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# To Study the Prevalence of Cholelithiasis in Patients with Type 2 Diabetes Mellitus in North Indian Population: A Case Control Study

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## ABSTRACT

**Background:** Diabetes Mellitus is the fifth leading cause of death globally. Liver disease is one of the leading cause of death in persons with Type 2 Diabetes Mellitus (T2DM) (1). T2DM is considered as a risk factor for gallstone disease. Cholelithiasis is associated with such risk factors as ageing, obesity, female sex genetic predisposition, alcohol abuse, hypercholesterolemia (2). Aims and objectives: 1.To study the Prevalence of Cholelithiasis in Patients with Type 2 Diabetes Mellitus in North Indian Population. **Methods:** All Patients presenting to OPD with diagnosis of T2DM from January 2017 to December 2018 with Cholelithiasis were included in the study. Diagnosis of Cholelithiasis was verified on clinical data, gall bladder wall thickness and ultrasonography. **Results & Conclusion:** There is higher prevalence of gall stone disease compared to controls however gall stone disease is multifactorial and only NIDDM females was an independent risk factor. Increasing age, female sex, genetic predisposition, hypercholesterolemia with low HDL cholesterol and higher BMI are independently associated with gall stones.

***Keywords:*** Cholelithiasis, Diabetes Mellitus.

## INTRODUCTION

Diabetes Mellitus is the fifth leading cause of death globally. Liver disease is one of the leading cause of death in persons with Type 2 Diabetes Mellitus (T2DM).[1] T2DM is considered as a risk factor for gallstone disease. Cholelithiasis is associated with such risk factors as ageing, obesity, female sex genetic predisposition, alcohol abuse, hypercholesterolemia.[2] Diabetic patients with biliary track stone disease have high serum lipids and bile concentrations of cholesterol. Thomas-Hofmann Index which characterises bile saturation with cholesterol is significantly higherin patients with Cholelithiasis and T2DM than in healthy individuals.[3] The prevalence of hepatobiliary disesase is increased in patients with diabetes whereas in T2DM diabetes is an independent risk factor for Chlelithiasis in females with IDDM.[4] The principal gall bladder pathologic feature in diabetic patients is a functional deficit creating a large, flaccid, poorly emptying organ. Cholecystitis seems to be more serious with worse infectious sequelae and more rapid disease progression in diabetics. Although the risk of cholecystectomy in diabetics is similar to that in non diabetics the complication rate for operations upon the biliary track in patients with biliary track is increased.[5] The prevalence of cholelithiasis in general population aged 30 years or more was 5-8% where as in patients with T2DM prevalence ranges from 16-22%. From clinical viewpoint T2DM combined with gallstones may induce acute cholecystitis more often and have higher chance of complications.[6] In this study we analyse the clinical and laboratory features of the pathology of gall bladder in patients with T2DM.

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## MATERIALS AND METHODS

All Patients presenting to OPD with diagnosis of T2DM from January 2017 to December 2018 with Cholelithiasis were included in the study. Diagnosis of Cholelithiasis was verified on clinical data, gall bladder wall thickness and ultrasonography .Patients were considered to be diabetic as defined by American Diabetes Association (ADA) criteria. ADA criteria for diagnosis of diabetes mellitus which is: Serum Hb A1C ≥6.5%.The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay

OR Fasting plasma glucose (FPG) ≥126 mg/dL (7.0 mmol/L). Fasting is defined as no caloric intake for at least 8 h. OR 2-h FPG ≥200 mg/dL (11.1 mmol/L) during an OGTT. The test should be performed as described by the WHO, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water. OR In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥200 mg/dL (11.1 mmol/L). Among diabetics, the above criteria were considered to include the patients for the study.The cases and controls were matched for age, gender and BMI.

**Inclusion criteria for case selection:**

1) Urine sugar – positive 2) FPG > 126 mg/dl 3) Clinically and ultrasonographically documented cholelithiasis.

**Exclusion criteria for case selection:**

1) Patients with congestive cardiac failure, urinary tract infection.
2) Ketonuria
3) Pregnant patients.

## RESULTS

504 patients were evaluated, 352 (70%) were females and 152 (30%) males with a gender ratio of 1:2.33. 90 (17.8%) patients had cholelithiasis. Among controls out of 500 examined patients 43 (8.6%) had cholelithiasis, higher number of attacks were noted among cases (81 attacks) as compared to controls (34 attacks). Also higher rate of complication was noted among cases (1.5%) among controls complication rate was much lower(0.4%). The common complaints were general weakness, dyspepsia, heartburn, right hypochondriac pain, abdominal distention and constipation. Hepatomegaly was noted in 252(50%) patients, gall bladder was increased in size in 75 (15%) patients, gall bladder perforation and emphysematous cholecystitis was noted in 5 (1%) patients each.

**Table 1: Distribution Of Patients As Per Attacks And Complications Of Cases**

| | Cases (T2 DM With Cholelithiasis) | Number Of Attacks | Number Of Complications |
|---|---|---|---|
| Male | 27 | 14 | 2 |
| Female | 63 | 67 | 6 |
| Total | 90 | 81 | 8 |

**Table 2: Distribution of Patients as Per Attacks and Complications of Controls.**

| | Cases (T2 DM With Cholelithiasis) | Number of Attacks | Number of Complications |
|---|---|---|---|
| Male | 1 | 31 | 0 |
| Female | 3 | 3 | 2 |
| Total | 4 | 34 | 2 |

## DISCUSSION

This was a hospital based case control study in which Prevalence of Cholelithiasis was assessed in Patients with T2DM. In this study, we found that there is increased Prevalence of Cholelithiasis among patients suffering from T2DM (90 Patients vs 4 Patients). A study by Ikard concluded that there is no proof that diabetic patients have more gallstones but suggested that the risk of acute cholecystitis in diabetic patients with gallstones is probably significant enough to warrant the performance of early cholecystectomy.[5] A European prospective study by Weikert et al. reported that persons with T2DM had an increased risk of occurrence of gallstones.[7] The probable reason could be insulin resistance which contributes to gallstone formation as exemplified by the study of Biddinger et al.[8] Obesity leads to insulin resistance and increased cholesterol secretion into bile which offsets the equilibrium between cholesterol,[8] lecithin, and bile salts resulting in crystallization of cholesterol forming gallstones. Other reasons could be our study design and less number of patients.

Most of our study patients belonged to reproductive age group which is in agreement with the findings of Agunloye et al.[9] and Schirmer et al.[10] Our study revealed that females are more predisposed to the development of gallstones (female = 71.0%, male = 29.0%) which is similar to the findings of Schirmer et al.[10] however, Agunloye et al. did not find any gender predilection. Our patients belong to the lower and middle socioeconomic strata as per the Kuppuswamy classification, and our study did not show any association between the diabetic status and socioeconomic status. Agunloye et al.[9] concluded that there is no concrete evidence or strong association between gallstone disease and social factors and educational status.

In our endeavor to find relation between the severity of gallstones (in the form of solitary/multiple; size of the largest gallstone) and HbA1c, we did not find any statistically significant relationship. Since cholelithiasis is a multifactorial disorder, mere blood glucose concentration as determined by HbA1c may not explain the number and size of gallstones.

## CONCLUSION

There is higher prevalence of gall stone disease compared to controls however gall stone disease is multifactorial and only NIDDM females was an independent risk factor. Increasing age, female sex, genetic predisposition, hypercholesterolemia with low HDL cholesterol and higher BMI are independently associated with gall stones.

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