Original Article

Observational study on the prevalence of diabetes mellitus among ultrasonographically diagnosed cholelithiasis patients

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Abstract

Background and Aim: Diabetes and cholelithiasis are common diseases worldwide in this era of modern epidemics of non - communicable diseases. Studies revealed that diabetes is a risk factor for gallstones. Since both diseases are related to altered carbohydrate and lipid metabolism, we hypothesized that the vice-versa, i.e., gallstone disease can be a risk factor for the development of diabetes. The aim of this study was to find the prevalence of diabetes mellitus among ultrasonographically diagnosed cholelithiasis patients and to find any correlation between parameters of gallstones and diabetes mellitus.

Methods: This was a hospital-based observational study. A total of 31 gallstone patients belonging to both genders (male = 9, female = 22) and in the age group of 20–80 years were enrolled in the study. From ultrasound report, parameters noted were: size of gallbladder, solitary or multiple gallstones, and size of the largest gallstone. All patients were asked about history of diabetes mellitus, (if history of diabetes is present – whether the diabetes was diagnosed before or after cholelithiasis), monthly family income, education status, and occupation. Data obtained were subjected to appropriate statistical analysis. $P < 0.05$ was considered statistically significant.

Results: In this endeavor, we found that the prevalence of diabetes among cholelithiasis patients was only 35.48%; and of the 11 diabetic patients, 3 developed gallstones before the diagnosis of diabetes mellitus. Socioeconomic status did not have any bearing on the occurrence of diabetes and gallstones in our patients. Glycated hemoglobin levels did not correlate with the severity of gallstone disease which is assessed in the form of solitary/multiple stones and size of the largest gallstone.

Conclusion: There is no increased prevalence of diabetes among cholelithiasis patients. Our hypothesis of gallstones acting as risk for developing diabetes could not be proved.

Key words: Diabetes, gallstones, glycated hemoglobin

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INTRODUCTION

Cholelithiasis and diabetes are prevalent worldwide and many a times coexist in patients. Studies suggest that diabetes mellitus and hepatobiliary diseases are closely linked.[1] Findings from the current epidemiologic studies suggests that persons with diabetes mellitus are at increased risk of gallstone formation; however, obesity and hyperlipidemia may be confounding variables. On the other hand, gallstones may be associated with increased risk of diabetes.[2-5] An increased risk of gallstone formation has been reported in persons with hyperinsulinemia even before manifest diabetes has developed.[6] Not many Asian studies have been done to know that cholelithiasis may lead to an altered carbohydrate

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metabolism which might result in diabetes mellitus at a later stage. There is a paucity of such studies. On Google search, we did not find any such Indian study.

Gallstone disease in diabetes mellitus is influenced significantly by age, body mass index, and duration of the disease.[7] It has been well-demonstrated that the occurrence of gallstones increases with age, an estimated 20% of adults over 40 years of age and 30% of those over age of 70 have gallstones.[8] Gender is an important risk factor for the development of cholelithiasis as the prevalence of gallstones is higher in women than in men; female sex hormones are most likely to be responsible for the higher prevalence in women.[9] During the reproductive years, the female-to-male ratio is about 4:1, with the sex discrepancy narrowing in the older population to near equality. Hence, we hypothesized that gallstone disease may alter the metabolism which may modify glucose homeostatic mechanism that might act as a starting point or complement other risk factors for the development of diabetes. The purpose of this study was to determine the prevalence of type 2 diabetes mellitus in already diagnosed cholelithiasis patients, to know whether the diabetes was diagnosed before or after cholelithiasis, to correlate the severity of gallstones with metabolic control of diabetes, and to find an association of socioeconomic status with diabetes mellitus and cholelithiasis.

MATERIALS AND METHODS

The study was conducted in the Department of Physiology in collaboration with the Department of General Surgery of our institute. Data were collected between April 2014 and September 2014.

Diagnosis of cholelithiasis and diabetes mellitus

Diagnosis of gallstones was made based on the ultrasound report.

Patients with fasting blood sugar (FBS) levels ≥110 mg/dL or earlier diagnosis of diabetes mellitus but under treatment, and their FBS may or may not be in normal range. Metabolic control was assessed by the estimation of glycated hemoglobin (HbA1c) levels.

Patients

Thirty-one patients were recruited from the outpatient and inpatient department of General Surgery of our institute after taking written informed consent.

Inclusion criteria

Patients diagnosed with cholelithiasis after ultrasound examination, belonging to both genders, in the age group of 20–80 years.

All patients were asked about history of diabetes mellitus (whether the diabetes was diagnosed before or after cholelithiasis), hypertension, dyslipidemia, dietary habits, etc.

All the enrolled patients were enquired about their monthly family income, education status, and occupation. Scoring and classification into socioeconomic classes was as per "Kupppuswamy's socioeconomic status scale."[10]

Exclusion criteria

Patients with known history of chronic disorders such as bronchial asthma, ischemic heart disease, obstructive jaundice, liver disorder, and abdominal surgeries were excluded from the study. Furthermore, patients with a history of chronic alcoholism were excluded as it has a strong bearing on the hepatobiliary physiology.

The study was approved by the Institutional Review Board.

Biochemical parameters

Available investigation reports such as FBS, postprandial blood sugar, fasting lipid profile, and liver function tests were documented. A volume of 2 ml of venous blood sample was collected in vacutainers from all the patients and HbA1c was estimated using commercially available kits (M/S Excel Diagnostics Pvt. Ltd., Hyderabad, India) based on Ion Exchange Resin Method. Test was carried out as per the manufacturer's instruction which is based on the method described by Nathan *et al*.[11]

Ultrasound parameters

Parameters noted were size of gallbladder, solitary or multiple gallstones, size of the largest gallstone, diameters of intrahepatic bile ducts and common bile duct.

Statistical analysis of data

Data were analyzed using SPSS version 17.0 (SPSS Inc., Chicago, IL, USA). Student's *t*-test for scale data, Chi-square test for categorical data, and correlation statistics were performed. $P < 0.05$ was considered statistically significant.

RESULTS

Of the 31 patients recruited for the study, 9 were male and 22 were female. Figure 1 shows that more number of patients were between 30 and 55 years of age. Table 1 shows the demographic and study parameters. Of 11 diabetic patients, 8 developed diabetes well before the

diagnosis of gallstones and only 3 patients developed diabetes after the diagnosis of cholelithiasis. Table 2 shows correlation statistics. Size of the largest gallstone correlated with neither HbA1c ($r = 0.186$, $P = 0.317$) nor mean glucose level ($r = 0.191$, $P = 0.303$). The size of the largest gallstone did not differ significantly ($P = 0.706$) between the diabetic and nondiabetic groups [Table 3 and Figure 2].

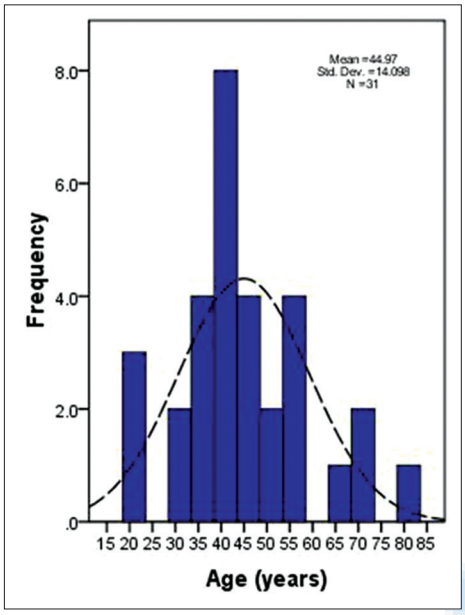

Figure 1: Age distribution of subjects

The number of gallstones (solitary/multiple) did not have any association with the diabetic status [Table 4, $P > 0.05$]. Furthermore, the prevalence of diabetes did not correlate with socioeconomic status.

DISCUSSION

This was a hospital-based, observational study in which diagnosed cases of cholelithiasis were assessed for the presence of diabetes mellitus and occurrence of

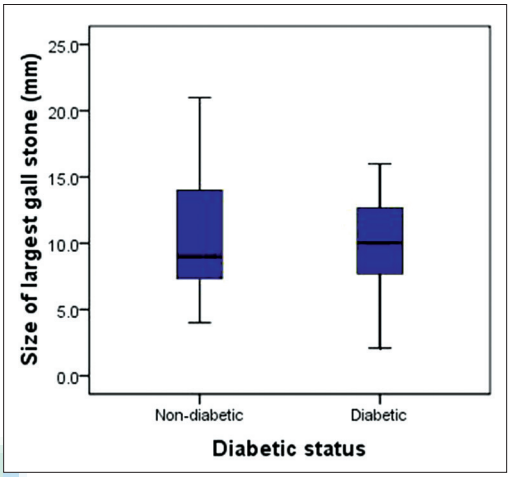

Figure 2: Difference in size of largest gallstone between nondiabetic and diabetic individuals

Table 1: Demographic and study parameters of the subjects

Parameter	Category	Minimum	Maximum	Mean	SEM	SD	*n*	Percentage
Age (years)		21	80	44.97	2.53	14.10	-	-
Gender	Male	-	-	-	-	-	9	29.0
	Female	-	-	-	-	-	22	71.0
Socioeconomic status	Upper-lower class	-	-	-	-	-	14	45.2
	Lower-middle class	-	-	-	-	-	14	45.2
	Upper-middle class	-	-	-	-	-	3	9.7
Diabetic status	Nondiabetic	-	-	-	-	-	20	64.5
	Diabetic	-	-	-	-	-	11	35.5
Random blood sugar (mg/dl)		78	353	146.23	12.21	68.0	-	-
HbA1c (%)		4.30	10.74	7.24	0.34	1.92	-	-
MBG (mg/dl)		35	326	163.13	15.53	86.44	-	-
Cholelithiasis	Absent	-	-	-	-	-	0	0.00
	Present	-	-	-	-	-	31	100.0
Gallstone	Solitary	-	-	-	-	-	9	29.0
	Multiple	-	-	-	-	-	22	71.0
Size of largest gallstone (mm)		2.1	21.0	10.31	0.76	4.26	-	-
Hypertension status	Normotensive	-	-	-	-	-	20	64.5
	Hypertensive	-	-	-	-	-	11	35.5
Ischemic heart disease status	No	-	-	-	-	-	30	96.8
	Yes	-	-	-	-	-	1	3.2
Smoking status	No	-	-	-	-	-	26	83.9
	Yes	-	-	-	-	-	5	16.1
Alcohol consumption	No	-	-	-	-	-	30	96.8
	Yes	-	-	-	-	-	1	3.2
Weight (kg)		52	90	72.03	1.36	9	-	-
Height (cm)		145	176	164.19	1.38	7.67	-	-
BMI (kg/m^2)		17.99	35.16	26.84	0.62	3.46	-	-

SEM: Standard error of mean, SD: Standard deviation, *n*: Number of patients, HbA1c: Glycated hemoglobin, MBG: Mean blood glucose, BMI: Body mass index

Table 2: Correlation statistics between various parameters

	Random blood sugar (mg/dl)	HbA1c (%)	Size of largest gallstone (mm)	Weight (kg)	Height (cm)	BMI (kg/m^2)	MBG (mg/dl)
Random blood sugar (mg/dl)							
r	1	0.398*	−0.212	0.111	0.261	−0.127	0.392*
P		0.027	0.253	0.553	0.156	0.495	0.029
HbA1c (%)							
r	0.398*	1	0.186	−0.018	−0.172	0.094	0.995**
P	0.027		0.317	0.922	0.355	0.617	0.000
Size of largest gallstone (mm)							
r	−0.212	0.186	1	−0.089	−0.215	0.098	0.191
P	0.253	0.317		0.633	0.246	0.598	0.303
Weight (kg)							
r	0.111	−0.018	−0.089	1	0.168	0.685**	−0.016
P	0.553	0.922	0.633		0.365	0.000	0.934
Height (cm)							
r	0.261	−0.172	−0.215	0.168	1	−0.600**	−0.164
P	0.156	0.355	0.246	0.365		0.000	0.378
BMI (kg/m^2)							
r	−0.127	0.094	0.098	0.685**	−0.600**	1	0.091
P	0.495	0.617	0.598	0.000	0.000		0.626
MBG (mg/dl)							
r	0.392*	0.995**	0.191	−0.016	−0.164	0.091	1
P	0.029	0.000	0.303	0.934	0.378	0.626	

*Significant at the 0.05 level (two-tailed), **Significant at the 0.01 level (two-tailed). HbA1c: Glycated hemoglobin, MBG: Mean blood glucose, BMI: Body mass index

Table 3: Difference between the diabetic and nondiabetic in relation to size of the largest gallstone

Group statistics					
Parameter	**Diabetic status**	***n***	**Mean**	**SD**	**SEM**
Size of largest gallstone (mm)	Nondiabetic	20	10.525	4.5278	1.0124
	Diabetic	11	9.907	3.8885	1.1724

Independent samples *t*-test									
Parameter	**Levene's test for equality of variances**		***T*-test for equality of means**					**95% CI of the difference**	
	F	**Significance**	***t***	**df**	**Significance (two-tailed)**	**Mean difference**	**SE difference**	**Lower**	**Upper**
Size of largest gallstone (mm)									
Equal variances assumed	0.640	0.430	0.381	29	0.706	0.6177	1.6209	−2.6974	3.9328
Equal variances not assumed			0.399	23.575	0.694	0.6177	1.5491	−2.5824	3.8179

SD: Standard deviation, SEM: Standard error of mean, CI: Confidence interval

diabetes before or after the diagnosis of cholelithiasis. In this study, we did not find any increased prevalence of diabetes among patients suffering from gallstones (diabetes = 35.5%, nondiabetic = 64.5%), which is in agreement with the findings of Ikard.[12] A study by Ikard also 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. On the contrary, a European prospective study by Weikert *et al*.[3] reported that persons with gallstones had an increased risk of type 2 diabetes and the occurrence of gallstones appeared to predict diabetes independent of obesity, hypertension, glucose, triglycerides, total cholesterol and established lifestyle risk factors for diabetes. In our study, of the 11 diabetic patients, 8 developed diabetes well in advance of the occurrence of gallstones and only 3 patients were diagnosed with diabetes after the development of cholelithiasis which is not in consonance with our research hypothesis and the findings of Weikert *et al*.[3] The probable reason could be insulin resistance which contributes to gallstone formation as exemplified by the study of Biddinger *et al*.[13] Obesity leads to insulin resistance and increased cholesterol secretion[13] into bile which offsets the equilibrium between cholesterol, 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*.[7] and Schirmer *et al*.[8] Our study revealed that females are more predisposed to the development of gallstones

Table 4: Difference between the diabetic and nondiabetic in relation to number of gallstones

Chi-square test			
Diabetic status	**Observed *n***	**Expected *n***	**Residual**
Nondiabetic	20	15.5	4.5
Diabetic	11	15.5	−4.5
Total	31		
Gallstone	**Observed *n***	**Expected *n***	**Residual**
Solitary	9	15.5	−6.5
Multiple	22	15.5	6.5
Total	31		
Test statistics	**Diabetic status**	**Gallstone**	
χ^2	2.613[a]	5.452[a]	
df	1	1	
Asymptotic significance	0.106	0.020	

[a]0 cells (0%) have expected frequencies <5, the minimum expected cell frequency is 15.5

(female = 71.0%, male = 29.0%) which is similar to the findings of Schirmer *et al*.[8] that male-to-female ratio is 4:1; however, Agunloye *et al*.[7] 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*.[7] 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.

Limitations of the study

The sample size of our study was small. We would like to recruit more patients in future and know the trends whether it is same or in accordance with our theory. Furthermore, a prospective cohort study can be designed to test our hypothesis.

CONCLUSION

We conclude that there is no increased prevalence of diabetes among cholelithiasis patients. We could not prove that the gallstones increases the risk of development of diabetes. There is no relationship of the two diseases, i.e., diabetes and gallstones with the socioeconomic status. The metabolic control of diabetes (HbA1c, mean blood glucose) did not correlate with the severity of gallstones (solitary/multiple or size of the largest gallstone).

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Conflicts of interest

A portion of this study was presented at OSMECON 2015, Osmania Medical College, Hyderabad, India, held from August 26, 2015 to August 28, 2015.

REFERENCES

1. Chen CH, Huang MH, Yang JC, Nien CK, Etheredge GD, Yang CC, *et al.* Prevalence and risk factors of gallstone disease in an adult population of Taiwan: An epidemiological survey. J Gastroenterol Hepatol 2006;21:1737-43.
2. Iasu YT, Kebede T. The association of diabetes mellitus with cholelithiasis and liver diseases in Addis Ababa – Ethiopia. East Cent Afr J Surg 2012;17:70-6.
3. Weikert C, Weikert S, Schulze MB, Pischon T, Fritsche A, Bergmann MM, *et al.* Presence of gallstones or kidney stones and risk of type 2 diabetes. Am J Epidemiol 2010;171:447-54.
4. Ruhl CE, Everhart JE. Association of diabetes, serum insulin, and C-peptide with gallbladder disease. Hepatology 2000;31:299-303.
5. Haffner SM, Diehl AK, Mitchell BD, Stern MP, Hazuda HP. Increased prevalence of clinical gallbladder disease in subjects with non-insulin-dependent diabetes mellitus. Am J Epidemiol 1990;132:327-35.
6. Misciagna G, Guerra V, Di Leo A, Correale M, Trevisan M. Insulin and gall stones: A population case control study in southern Italy. Gut 2000;47:144-7.
7. Agunloye AM, Adebakin AM, Adeleye JO, Ogunseyinde AO. Ultrasound prevalence of gallstone disease in diabetic patients at Ibadan, Nigeria. Niger J Clin Pract 2013;16:71-5.
8. Schirmer BD, Winters KL, Edlich RF. Cholelithiasis and cholecystitis. J Long Term Eff Med Implants 2005;15:329-38.
9. Novacek G. Gender and gallstone disease. Wien Med Wochenschr 2006;156:527-33.
10. Park K, editor. Medicine and social sciences. In: Park's Textbook of Preventive and Social Medicine. 22nd ed. Jabalpur, India: Banarsidas Bhanot; 2013. p. 640-1.
11. Nathan DM, Singer DE, Hurxthal K, Goodson JD. The clinical information value of the glycosylated hemoglobin assay. N Engl J Med 1984;310:341-6.
12. Ikard RW. Gallstones, cholecystitis and diabetes. Surg Gynecol Obstet 1990;171:528-32.
13. Biddinger SB, Haas JT, Yu BB, Bezy O, Jing E, Zhang W, *et al.* Hepatic insulin resistance directly promotes formation of cholesterol gallstones. Nat Med 2008;14:778-82.