

Prevalence and Risk Factors of Asymptomatic Gall Stone in Patient with Type 2 Diabetes Mellitus

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Abstract: ***Aims:** To study the prevalence of asymptomatic gall stone in type 2 diabetes mellitus. To study the relationship of Risk Factors with gall stone disease. . **Material & Method:** The present study was conducted on 100 diabetic subjects, out of which 62 were males and 38 were females. All the patients were diagnosed case of Type 2 diabetes mellitus patient or newly detected Type 2 diabetes mellitus patients which admitted in J.A. Group of Hospitals and who attend Medicine OPD were included. BMI measurement and ultrasound examination to find gallstone was done. Blood samples were taken for HbA1C, FBS, Lipid profile and the association between duration of diabetes, lipid levels, FBS, with gallstone was evaluated. **Results:** prevalence rate of asymptomatic gallstone found to be 26% in diabetic patients. 65.38% were females other hand only 34.16% male patients have gall stone (P= 0.001). Among the female patients with asymptomatic gall stone 52% was multiparous and 30.76% was primiparous (P=0.02). The mean BMI (body mass index) of study group with gall Stone Age 27.77± 3.29. It shows that there is a very significant positive correlation of BMI with the incidence of gall stone in diabetic population (P value 0.01). Among patient with dyslipidemia and gall stone 73.07% have hypertriglyceridemia followed by raised LDL (42.30%) and raised total cholesterol (34.61%) but On statically analysis it is found that serum triglyceride and serum cholesterol level shows positive correlation with incidence gall stones. (P=0.002 & P= 0.01 respectively) **Conclusion:** The prevalence of asymptomatic gallstones in middle-aged and elderly patients with type 2 diabetes mellitus is high. Female, total cholesterol, and BMI were risk factors for asymptomatic gallstones in middle-aged and elderly patients with type 2 diabetes mellitus.*

Keywords: BMI, Female, multiparous, cholesterol, triglyceride

1. Introduction

Gallstone disease (GSD) is one of the most common and costly digestive diseases worldwide, and it is more prevalent in Europe and America than in Asia and Africa. Approximately 6-44% of the general population have gall stones most of which are asymptomatic. More recent study disclose that only 10-80% of asymptomatic patients ever develop symptoms. Recently study from South India have highlighted pigment and mixed variety of gall stone to be common. In contrast to cholesterol stones reported from north east and western part of India. A number of factors, including old age, female gender, genetics, diet, obesity, diabetes, and the use of oral contraceptives or hormone therapy, have been associated with increased risk of GSD [1]. Many studies from around the world reported an increased prevalence of Gallstone in patients with DM. Although the association between diabetes mellitus (DM) and gallstones is controversial, many studies revealed that diabetic patients are two to three times more risky for gallstones than nondiabetics [2]. Diabetes was reported to be frequently associated with inflammation of biliary tract and cholelithiasis [3]. The definite cause of gallstones in diabetics is not well clarified. However, due to autonomic neuropathy, the contraction of gallbladder is poor resulting in hypomotility, impaired gallbladder emptying and biliary stasis [4, 5] resulting in increased gallbladder volume, which predispose to gallstones formation [6]. Obesity, hypertriglyceridemia [7], and hyperinsulinemia [8], which are frequently reported in diabetic patients, are proposed to be contributing factors for gallstones formation. There is relationship between the metabolic pathway of plasmatic cholesterol with bile cholesterol and bile acid proportion. Bile is the principal way for excreting body cholesterol. Therefore an association between plasma lipid concentration and gall stone disease have been suggested.

2. Materials and Methods

The present study was conducted in J A group of hospital, Gwalior, M.P. (G.R. Medical college, Gwalior, M.P.)

Study Design: The present study is a cross sectional study, conducted over a period of one year on 100 patients of type 2 diabetes mellitus without symptoms of gall bladder stone.

Inclusion Criteria:

- All diabetic patients attending JA group of hospital.
- Age more than 30 yrs.

Exclusion Criteria

- History of pain in right hypochondrial region of abdomen.
- History of alcohol consumption.
- Past history of gall stone.
- Past history of gall bladder surgery.
- Family history of gall stone.
- LFT deranged.
- History of taking drug i.e. oral contraceptive pills, clofibrate and other fibrate, somatostatin analogues etc affecting liver.

3. Method and Data Collection

All the diabetic patients attending JAH Groups of Hospital, Gwalior, M.P. were screened for eligibility. Informed consent was taken from the eligible patients and enrolled in the present study. The patients were interviewed and underwent thorough physical examination. Their Data comprising of name, age, sex, personal, occupational and proper history was recorded on the proforma. All patients were evaluated on the basis of clinical, haematological and ultrasono graphically. A detailed history was elicited from

all patients with emphasis on symptomatology and duration of diabetes mellitus.

Waist hip ratio: Waist circumference in centimeters is measure in the horizontal plane above the iliac crest. Hip circumference in centimeters at maximal circumference of buttock, and ratio of both calculated. Normal Waist hip ratio:- Male < 1.0, Female < 0.9.

Body mass index (BMI) was calculated according to Quetelet's formula and subjects were accordingly categorized.

Type	BMI (Kg/m ²)
Underweight	<18.5
Healthy weight	18.5-24.9
Overweight	25-29.9
Obese class I	30- 34.9
Obese Class II	35-39.9
Obese Class III	>40

Source: Adapted from National Institutes of Health, National Heart, Lung, and Blood Institute: *Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults*. U.S. Department of Health and Human Services, Public Health Service, 1998.

Investigations; All patients were subjected to the following investigation at the time of inclusion into the study. Routine hemogram, Glycosylated hemoglobin. (HbA1c), Fasting and post prandial blood sugar, Lipid profile(total cholesterol, triglycerides,LDL,HDL, VLDL),Blood urea and serum creatinine, Urine routine and microscopic examination, Serum bilirubin, SGOT , SGPT, Ultrasonography. **Lipid values were classified according to NCEP ATP III Guidelines** :-Total Cholesterol > 200 mg%, Triglyceride > 150 mg%, LDL >100 mg%, HDL < 40 mg%.

Statistical analysis; Data was analysed using Microsoft excel, the software statistics calculator, described data was analysed using student's t test. Two tailed P value <0.05 was considered significant.

4. Results

Table 1: Sex distribution of Gallstone patients in study population

Gallstone	Male		Female		Total	
	No.	%	No.	%	No.	%
Present	9	34.61	17	65.38	26	26
Absent	53	71.62	21	28.37	74	74
Total	62		38		100	

Above table show that among patient with gall stone, 65.38% were females other hand only 34.16% male patients

have gall stone. On statistically analysis of the data clear that female gender has significant positive correlation with the incidence of gall stone in diabetes population. (P= 0.001)

Table 2: Parity of Gallstone female patients in study population

Parity	No. of Patients	Percent	Total
Nulli parous	0	0	0
Primi parous	4	30.76	4
Multi parous	13	52	13

Among the female patients with asymptomatic gall stone 52% was multiparous and 30.76% was primiparous this shows positive correlation of parity of female patients with the occurrence of gall stone in type 2 diabetes. (P=0.02)

Table 3: Body mass index (BMI) of Gallstone patients in study population

BMI	Male		Female		Total	
	No.	%	No.	%	No.	%
normal (18-24.9)	1	11.11	2	11.76	3	11.53
Overweight (25-29.9)	8	88.88	11	64.70	19	73.07
obese (>30)	0	0	4	23.52	4	15.38
Total	9		17		26	

Above table shows that both in males and females with gall stone majority are overweight (BMI 25-29.09) Constituting an average of 73.07% of the study population. The mean BMI of study group with gall Stone Age 27.77± 3.29. On statistically analysis correlation of BMI with incidence of gall stone, it shows that there is a very significant positive correlation of BMI with the incidence of gall stone in diabetic population. (P value 0.01)

Table 4: Lipid Profile of Gallstone patients in study population

Lipid profile	Male		Female		Total	
	No.	%	No.	%	No.	%
↑ Total cholesterol	3	33.33	6	35.29	9	34.61
↑ Triglyceride	7	77.77	12	70.58	19	73.07
↑LDL	2	33.33	2	47.05	4	42.30
↓ HDL	3	22.22	8	11.76	11	15.38

Among patient with dyslipidemia and gall stone 73.07% have hypertriglyceridemia followed by raised LDL (42.30%) and raised total cholesterol (34.61%).The mean serum triglyceride level of the study group with gall stone is 193.19± 62.44 mg / dl, The mean total cholesterol is 190.76± 62.12 mg / dl the mean LDL is 129.14 ± 66.88 mg/dl and the mean HDL value is 49.21± 12.74 mg / dl. On statically analysis it is found that serum triglyceride and serum cholesterol level shows positive correlation with incidence gall stones. (P=0.002 & P= 0.01 respectively)

Table 5: Co-relation of Clinical and Biochemical Parameters of Gall stone Patients in Type 2 Diabetes Mellitus

Parameter	Gall stone	Mean	Standard deviation (SD)	P value	Inference
Sex	Present			0.001	S
	Absent				
Age	Present	53.65	11.58	0.83	NS
	Absent	54.20	11.10		
Parity	Present	2.88	1.53	0.02	S
	Absent	1.90	0.99		
BMI	Present	27.77	3.29	0.01	S
	Absent	25.85	3.30		
Waist Hip ratio	Present	1.09	0.15	0.06	NS
	Absent	1.03	0.14		
Fasting Blood Sugar (FBS)	Present	140.07	24.90	0.77	NS
	Absent	142.29	36.77		
Post Prandial Blood sugar (PPBS)	Present	235.4	51.64	0.57	NS
	Absent	227.61	63.05		
HbA1c	Present	9.72	2.78	0.57	NS
	Absent	9.40	2.35		
Duration of Type 2 Diabetes Mellitus	Present	4.60	3.02	0.20	NS
	Absent	5.72	4.08		
TC	Present	190.76	62.12	0.01	S
	Absent	157.55	57.20		
TG	Present	193.49	62.44	0.002	S
	Absent	139.08	60.93		
LDL	Present	129.14	66.88	0.30	NS
	Absent	100.64	48.34		
HDL	Present	49.21	12.74	0.97	NS
	Absent	49.100	17.33		

S = Significant, NS = Not Significant

There is significant difference between presence and absence of Gall stone in Sex, Parity, MI Total Cholesterol and Triglyceride level with p value of 0.001, 0.02, 0.03, and 0.0001 respectively. There is no significant difference found between presence and absence of Gall stone with reference to Age, WHR Fasting Blood Sugar, PPBS, HbA1c, Duration of Diabetes, LDL and HDL.

5. Discussion

Prevalance:- Various study shows different rate of prevalence of gall stone diseases in Type 2 Diabetes Mellitus patients. **Goyal Ket et al** [9] studied the magnitude of asymptomatic gall stone diseases in patients of Type 2 Diabetes Mellitus patients in Delhi and found about 31% have asymptomatic diseases. **Saxena R et al** [10] also studied the prevalence of gall bladder stones Type 2 Diabetes Mellitus patients in their correlation they found that 29% of Type 2 Diabetes Mellitus patients have ultrasonographic evidence gall stone as compare to 3.7% of healthy subject. Another study was done by **Malik et al** [11] and reported 12.77% prevalence of gall stone in 329 Type 2 Diabetes Mellitus patients. In our present study the prevalence of asymptomatic gall stone diseases in patients with Type 2 Diabetes Mellitus was found to be 26%.

Gender:- **Elmehdawi RR et al** [12] studied 161 Type 2 Diabetes Mellitus patients and found that the prevalence of gall bladder stone was significantly higher in female patients and the result was statically significant too. **Anmar H et al** [13] also conducted a clinical study in Type 2 Diabetes Mellitus patients to find out any association between gall stone and Type 2 Diabetes Mellitus. Their study revealed that the incidence gall significantly higher in female diabetic

patients. The study done by **Saxena R et al** [10] also shows that 67.5% of the diabetic patients with gall stone disease were female, Revealing a statically significant positive correlation. In our study also among those with Gall stone and Diabetes 65.38% were female and 34.61% were males which on statistical analysis showed significant positive correlation (P=0.001)

Parity:- **Chapman et al** [14] studied the prevalence of gall bladder stone in Type 2 Diabetes Mellitus and found that in female patient Diabetes and gall stones, as the parity increases the prevalence of gall stone also increases and the result was found to be significant. **Elmehdawi RR et al** [12] show that the mean number of pregnancy of diabetic women gall stone diseases was significantly higher when compared with those without gall stone diseases showing a positive correlation (P=<0.05). Our study also similar with above studies. In our female study group it was showed that as the parity increases the incidence of gall stone also increases, with the positive correlation (P=0.02) which is statistically significant.

BMI:- **Elmehdawi RR et al** [12] shows that obesity was more prevalent in diabetics with gall bladder stone. Diabetics and gall stone had significantly higher BMI than those without stone. The mean BMI of those with gall stone was 34.78 ± 6.29 is their study. **Tao-Hsin Tung et al** [15] also studied the correlation of BMI of Diabetes and gall stone diseases and they found that BMI was significantly correlated with gall stone diseases and Diabetes. The mean BMI they found out was 26.57 ± 1.07 . In our study the mean BMI of the study group with gall stones was 27.77 ± 3.29 and BMI incidence a significant positive correlation with the incidence of gall stone is diabetes population P=0.01.

Lipid Profile:- **Tao-Hsin Tung et al** [15] show the mean total cholesterol 220.09 ± 20.59 mg/dl, which is significantly associated with gall stone disease in type 2 diabetes $p=0.00$. But the mean triglyceride was 178.50 ± 38.95 is not statistically significant. **Bhika Ram et al** [16] studied the relation Gall stone disease and diabetic, found that dyslipidemia was present in 81% of study group. The most common abnormality found out washypercholesterolemia followed by hypertriglyceridemia and raised LDL. Our study show 73.07% have hypertriglyceridemia followed by increased LDL in 42.85% and increased total cholesterol in 34.61%. But on statistical analysis significant correlation seen with hypertriglyceridemia and hypercholesterolemia with the incidence of gall stone in type2 diabetes mellitus patient. (P value 0.0001 and 0.03 significantly)

This study had some limitations also. As the sample size was small, the statistical power of the study may not be adequate enough to apply for a large population. Because of the cross sectional nature of the study, the casual association of risk factors and the disease cannot be established. As gall stone disease can be caused by variety of other factors the involvement of confounding factors in the study cannot be excluded completely.

6. Conclusion

Diabetes mellitus and gall bladder stone are both common and correlated disease. Various modifiable and no modifiable risk factors are also correlated with the association of type 2 diabetes mellitus and gall stones. Among the non modifiable risk factors female sex holds a strong predisposition and especially multiparous women. The other modifiable risk factors which were found to be significant on the study were BMI, hypertriglyceridemia and hypercholesterolemia. The importance of this study lies in the fact that, this was conducted among asymptomatic diabetic patients this warrants the role of early screening of type 2 diabetes mellitus asymptomatic patients and the abnormal lipid, body mass index and waist hip ratio should be considered as alarming factor for gall stone thus helping in early detection and avoidance of complications in the future, along with aggressive management of modifiable risk factors.

References

- [1] Jorgensen T. Epidemiology and gallstones Ugeskr Laeger. 2005; 167(24):2610-3.
- [2] Pazzi P, Scagliarini R, Gamberini S, Pezzoli A. Review article: gall-bladder motor function in diabetes mellitus. Aliment Pharmacol Ther. 2000; 14Suppl 2:62-65.
- [3] Liu CM, Tung TH, Liu JH, Lee WL, Chou P. A community-based epidemiologic study on gallstone disease among type 2 diabetics in Kinmen, Taiwan. Dig Dis 2004; 22:87-91.
- [4] Kayacetin E, Kisakol G, Kaya A, Akpınar Z. Real-time sonography for screening of gallbladder motility in diabetic patients: relation to autonomic and peripheral neuropathy. Neuro Endocrinol Lett. 2003; 24(1-2): 73-76.
- [5] Keil R. The gall bladder, biliary tract, and diabetes mellitus. VnitrLek. 2004; 50(5): 383-385.
- [6] Olokoba AB, Bojuwoye BJ, Olokoba LB, Wahab KW, Salami AK, Braimoh KT, et al. The relationship between gallstone disease and gall bladder volume. Niger J Clin Pract. 2008; 11(2): 89-93.
- [7] Acharya SK. Diabetes mellitus and gastrointestinal system. In: Tripathy BB, Chandali HB, Das AK, Rao PV, Madhu SV, Mohan V (Eds). Rssdi: Textbook of Diabetes Mellitus, Vol. 2, Jaypee Brothers Medical Publishers, 2012: pp: 939-949.
- [8] Ruhl CE, Everhart JE. Association of diabetes, serum insulin, and C-peptide with gallbladder disease. Hepatology 2000;31: 299-303
- [9] Goyal K et al: asymptomatic gall stone diseases in patients of Type 2 Diabetes Mellitus APICON 2011, pg 52.
- [10] Saxena R, Sharma S, Dubey DC. Gallbladder Disorder in Type 2 Diabetes Mellitus Cases. J Hum Ecol 2005;18(3):169-71.
- [11] Malik GM, Jeelani GH et al.: Ultrasonographic survey of gall stones amongst diabetic patients of Kashmir. Ind Jr of Gastroenterology 1999 Nov; 18(suppl 2).
- [12] Elmehdawi RR et al Prevalence of Gall Bladder Stones among Type 2 Diabetic Patients in Benghazi Libya: A Case-control Study Libyan J Med, AOP: 081122 pg 23-28
- [13] Anmar H et al: Association between gallstone and diabetics type 2 Iraqui patients Iraqui J Pharm Sci Vol20 (2) 2011;38-43.
- [14] Chapman BA, Wilson IR, Frampton CM, et al. Prevalence of gallbladder disease in diabetes mellitus. Dig Dis Sci. 1996; 41(11):2222-8.
- [15] Tao-Hsin Tung et al A population-based follow-up study on gallstone disease among type 2 diabetics in Kinmen, Taiwan World J Gastroenterol 2006 July 28; 12(28): 4536-4540.
- [16] Bhika ram et al: frequency of Gall stones in patients with Diabetes Mellitus (A hospital based multidisciplinary study).Medical channe April-June 2012 Vol.16,no2;230-232.