

A prospective case control assessment of the gall bladder volume in type 2 diabetes mellitus patients using real time ultrasonography

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Abstract

Aim: To assess the gallbladder volume in T2DM patients and in healthy controls by using Ultrasonography.

Methodology: This cases control study was conducted among 55 diabetic patients enrolled from the diabetes clinic of the RVM Institute of Medical Sciences & Research Centre, Laxmakapally, Telangana, India and 55 healthy patients (control group). 30-60 year patients of type 2 diabetes mellitus diagnosed since 5 year or more and functioning gall bladder with well controlled blood sugar levels. The diagnosis of diabetes in these patients was in accordance with WHO criteria i.e., fasting plasma glucose level ≥ 126 mg/dl, and ≥ 200 mg/dl plasma glucose level after 2hr of ingestion of standardised 75 gm glucose. An informed consent was taken from all the subjects in the study and control groups. All the patients were randomly selected for the study among patients regularly attending diabetic clinic of this hospital and following our criteria's of selection.

Results: Mean age of diabetic Patient was 48.5 years in study group and 53 years in control group. 45.5% of diabetics were males and remaining 54.5% were females, whereas in control group male to female ratio was equal, means 49% males and 50% females. 85.5% cases in control group had no gall bladder disease, while only 63.6% cases in group with diabetes had no gall bladder disease. In group with DM type 2, 20% had cholelithiasis, 9.1% had cholecystitis, and 7.3% had sludge: while in control group, 5.5% had cholelithiasis, 3.6% had cholecystitis, and 5.5% had sludge. The percentage of contraction of gall bladder had reduced markedly in chronic diabetics (45.6 ± 9.57) as compared to controls (65.2 ± 7.34) (p value-0.001). The fasting gall bladder volume in chronic diabetics was higher (43.47 ± 5.35) than that of controls (28.45 ± 4.26) and the difference of values was found to be highly significant (p value 0.001).

Conclusion: In patients of diabetes mellitus type 2, higher fasting gall bladder volume and decreased percentage of contraction are observed. Therefore, all T2DM patients should be evaluated using ultrasonography for the presence of increased fasting gallbladder volumes to assess the risk of progression to gall stone disease.

Keywords: Diabetes mellitus, USG, gall stone, volume

Introduction

Diabetes mellitus (DM) is an irreversible syndrome of chronic hyperglycemia due to relative insulin deficiency, resistance, or both^[1]. Diabetes is broadly classified into type 1 and type 2. Type 2 is the most common type accounting for at least 90% of cases^[1,2].

The current prevalence of DM in Nigeria is estimated to be about 8-10%^[3]. In addition to the other complications seen in type 2 DM, they also suffer from autonomic neuropathy, which affects the motility and function of the digestive system including the gallbladder (GB) whose functions are regulated by the autonomic nervous system^[1,3,4].

Reduced motility of the GB causes GB hypotonia, the stasis of bile which provides a nidus for stone formation and infection^[4,5]. Studies in literature have reported a high prevalence of GB disorder in diabetics compared with the general population, a development which has been hypothesized to result from impairment of GB contractility complicating diabetic vagal neuropathy^[4-7].

Real-time ultrasonography is the dominant screening method for GB evaluation and the aim of this study was to sonographically evaluate the GB in patients with type 2 DM and compare the findings with a non-diabetic control group (age and sex matched)^[8]. Dodds *et al.* in 1985 calculated GB volume using a simple ellipsoid method using the following formula: $V = \pi/6 (L \times B \times H)$, where L is length, W is the width, and H is the height or anteroposterior (AP) dimensions of the GB; the constant $\pi/6$ has a value of 0.523, where π is a constant (22/7)^[9]. Chapman *et al.* in 1998 also compared GB volume in diabetics and control groups using ultrasonography^[10], which further corroborated the study by Dodds *et al.*^[9].

If patients with DM type 2 have an increased prevalence of gallstones and stasis is important in the pathogenesis, then a larger volume and reduced motility of gallbladder may be present in the patients with DM type 2 prior to the formation of gallstones.

Materials and Methods

This case control study was conducted among 75 diabetic patients enrolled at RVM Institute of Medical Sciences & Research Centre, Laxmakkapally, Telangana, India and 75 healthy patients (control group). The diagnosis of diabetes in these patients was in accordance with WHO criteria i.e., fasting plasma glucose level ≥ 126 mg/dl, and ≥ 200 mg/dl plasma glucose level after 2hr of ingestion of standardized 75 gm glucose.

An informed consent was taken from all the subjects in the study and control groups. All the patients were randomly selected for the study among patients regularly attending diabetic clinic of this hospital and following our criteria's of selection.

Inclusion criteria

- Age 30-60 year patients of.
- Type 2 diabetes mellitus diagnosed since 5 year or more.
- Functioning gall bladder with well controlled blood sugar levels.

Exclusion criterion

- Patients with history of pre-existing hepatobiliary or gastrointestinal disease.
- Taking antihypertensive drugs.
- Pregnant females.

Methodology

Gallbladder volume was measured in all the subjects after 12 hours overnight fasting by using a 3.5 to 5 MHz convex transducer in Wipro GE Voluson S6 and medison accuvix ultrasound and colour Doppler machine. The greatest length (L), maximum transverse width (W), and highest anteroposterior dimensions (H) were measured and documented. Gall bladder motility was observed by measuring fasting and post meal gallbladder volumes. Post meal volume was taken one hour after giving fatty meal i.e. four slice of bread with 30 gm butter. The percentage of gallbladder contraction was calculated by the formula ^[11]. The results of the study have been compiled, tabulated and statistically analyzed for comparisons.

Results

Mean age of diabetic Patient was 48.5 years in study group and 53 years in control group. 45.5% of diabetics were males and remaining 54.5% were females, whereas in control group male to female ratio was almost equal, 49.1% males and 50.9% females.

Table 1: Demographic details

Variables		Case group (n=55)		Control group (n=55)	
		Number	%	Number	%
Age (in years)	30-40	10	18.2	11	20
	41-50	19	34.5	17	30.9
	51-60	26	47.3	27	49.1
Gender	Males	25	45.5	27	49.1
	Females	30	54.5	28	50.9

In our study, higher prevalence of gall bladder disease in group of chronic diabetics is seen as compared to group of controls. 85.5% cases in control group had no gall bladder disease, while only 63.6% cases in group with diabetes had no gall bladder disease. In group with DM type 2, 20% had cholelithiasis, 9.1% had cholecystitis and 7.3% had sludge: while in control group, 5.5% had cholelithiasis, 3.6% had cholecystitis and 5.5% had sludge.

Table 2: Prevalence of gallbladder disease among study group & control group

Groups	No Gall bladder disease	Cholelithiasis	Cholecystitis	Sludge
Chronic Diabetic (n=55)	35 (63.6%)	11 (20%)	5 (9.1%)	4 (7.3%)
Controls (n=55)	47 (85.5%)	3 (5.5%)	2 (3.6%)	3 (5.5%)

The percentage of contraction of gall bladder had reduced markedly in chronic diabetics (46.62 ± 9.57) as compared to controls (66.21 ± 7.34) (p value- 0.001). The fasting gall bladder volume in chronic diabetics was higher (44.47 ± 5.35) than that of controls (29.45 ± 4.26) and the difference of values was found to be highly significant (p value 0.001).

Table 3: Percentage of contraction of gall bladder volume and Fasting gall bladder volume among study group & control group

Variables	Chronic Diabetic (n=55)	Controls (n=55)
Mean percentage of gall bladder contraction (%)	46.62 ± 9.57	66.21 ± 7.34
Mean fasting gall bladder volume (in CC)	44.47 ± 5.35	29.45 ± 4.26

Discussion

Diabetics in particular those with T2DM have an increased prevalence of gallstones ^[12].

Diabetic subjects are reported to have a two to three-fold increase in the prevalence of cholesterol gall stones^[13]. Diabetes mellitus is a growing health care problem worldwide and is characterised by metabolic abnormalities and complications involving kidneys, nerves, blood vessels and the gastrointestinal tract^[4].

The etiology of cholesterol gallstone disease is multifactorial. Carey and Small showed the importance of cholesterol supersaturation of bile and investigated cholesterol saturation index^[14]. After the finding of an elevated cholesterol saturation index in normal subjects, attention shifted to the nucleation time^[15] as a key factor in cholesterol stone formation and the identification of putative nucleation and anti-nucleating factors followed^[16-18]. Stasis of the gallbladder bile plays an important role in the development of cholesterol stones by providing the time necessary for the precipitation of cholesterol crystals^[23].

The main reasons for the high prevalence of gall stone disease in diabetes mellitus is due to decreased gall bladder motility, decreased postprandial cholecystokinin (CCK) release, decreased sensitivity of gall bladder smooth muscle to CCK, decreased number of CCK receptors in the gallbladder wall, supersaturation of bile, and the presence of gall stones themselves^[20, 21].

Gallbladder emptying in the diabetic population has been found to be decreased^[22, 23], however, this was not related to the presence or absence of diabetic neuropathy^[22]. These authors found that diabetic neuropathy has a subtle effect on gallbladder emptying^[22, 23] and the presence of obesity, type of diabetes, and blood glucose regulation did not affect the outcome^[23]. Even some studies revealed normal gallbladder emptying in patients with diabetes^[24, 25].

In our study, the percentage of contraction of gall bladder had reduced markedly in chronic diabetics (46.62 ± 9.57) as compared to controls (66.21 ± 7.34) (p value- 0.001). The fasting gall bladder volume in chronic diabetics was higher (44.47 ± 5.35) than that of controls (29.45 ± 4.26). Raman *et al.*^[26] who found the incidence of gallstones in diabetics to be 32% and that in healthy controls to be 6.7%. According to Stone *et al.*^[27] gallbladder emptying was lower in diabetics with gallbladder disease. In a study done by Raman *et al.*^[26], it was shown that percentage contraction of gallbladder was reduced in diabetes with gallbladder disease ($41.84 \pm 11.74\%$) as compared to controls ($53.07 \pm 16.31\%$) and diabetics without gallbladder disease ($48.74 \pm 11.75\%$). Similar findings were produced by Gaur *et al.*^[21], Pazzi *et al.*^[28], Yang *et al.*^[29] and Kayacetin *et al.*^[30]. Thus, the present study was clearly in concert with the above-mentioned studies.

Conclusion

In patients of diabetes mellitus type 2, higher fasting gall bladder volume and decreased percentage of contraction are observed. Therefore, all T2DM patients should be evaluated using ultrasonography for the presence of increased fasting gallbladder volumes to assess the risk of progression to gall stone disease.

References

1. Kumar PJ, Clark ML. Diabetes mellitus and other disorders of metabolism. Edinburg, Scotland: Saunders. Kumar & Clark's Clinical Medicine. Eighth Edition, 2012, 1001-1022.
2. Diabetes. <http://www.who.int/mediacentre/factsheets/fs312/en/2021>.
3. Diabetes mellitus in Nigeria: the past, present and future. Ogbera AO, Ekpebegh C. World J Diabetes. 2014;5:905-911.
4. Real time sonography for screening of gallbladder motility in diabetic patients: relation to autonomic and peripheral neuropathy. Kayacetin E, Kisakol G, Kaya A, Akpınar Z.

- <https://pubmed.ncbi.nlm.nih.gov/12743537/> Neuro Endocrinol Lett. 2003;24:73-76.
5. Gallstone disease and related risk factors in a large cohort of diabetic patients. Pagliarulo M, Fornari F, Fraquelli M, *et al.* Dig Liver Dis. 2004;36:130-134.
 6. Prevalence of gallbladder disease in diabetes mellitus. Chapman BA, Wilson IR, Frampton CM, Chisholm RJ, Stewart NR, Eagar GM, Allan RB. Dig Dis Sci. 1996;14:2222-2228.
 7. The relationship between gall-stone disease and gallbladder volume. Olokoba AB, Bojuwoye BJ, Olokoba LB, Wahab KW, Salami K, Braimoh KT, Inikori AK. Niger J Clin Pract. 2008;11:89-93.
 8. Diagnostic tests for gallbladder disease. Rodriguez D, Marcellin L, 2016, 1. <https://www.everydayhealth.com/gallbladder/diagnostic-tests-for-gallbladder-disease.aspx>.
 9. Sonographic measurement of gallbladder volume. Dodds WJ, Groh MJ, Darweesh RM, Lawson TL, Kishk SM, Kern MK. AJR Am J Roentgenol. 1985;145:1009-1011.
 10. Gallbladder volume: comparison of diabetics and controls. Chapman BA, Chapman TM, Frampton CM, Chisholm RJ, Allan RB, Wilson IR, Burt MJ. Dig Dis Sci. 1998;43:344-348.
 11. Gaur C, Mathur A, Agarwal A, Verma K, Jain R, Swaroop A. Diabetic autonomic neuropathy causing gall bladder dysfunction. The Journal of the Association of Physicians of India. 2000;48(6):603-5.
 12. Chapman TMBA, Chapman CM, Frampton RJ, Chisholm RB, Allan IR, Wilson. Gallbladder volume comparison of diabetics and controls. Digestive Dis Sci. 1998;43(2):344-348.
 13. Raman PG, Patel A, VM. Gall bladder disorder and Type 2 diabetes mellitus. A clinical based study. J Assoc. Phys. India. 2002;50:887-890.
 14. Carey MC, Small DM. The physical chemistry of cholesterol solubility in bile: relationship to gallstone formation and dissolution in man. J Clin Invest. 1978;61:998-1026.
 15. Holan KR, Holzbach RT, Hermann RE, *et al.* Nucleation time: a key factor in the pathogenesis of cholesterol gallstone disease. Gastroenterology. 1979;77:611-617.
 16. . Kibe A, Holzbach RT, LaRusso NF, *et al.* Inhibition of cholesterol crystal formation by apolipoproteins in supersaturated model bile. Science. 1984;225:514-516.
 17. Levy PF, Smith BF, Lamont JT. Human gallbladder mucin accelerates nucleation of cholesterol in artificial bile. Gastroenterology. 1984;87:270-275.
 18. Gallinger S, Taylor RD, Harvey PR, *et al.* Effect of mucous glycoprotein on nucleation time of human bile. Gastroenterology. 1985;89:648-658.
 19. Jazrawi RP, Pazzi P, Petroni ML, *et al.* Postprandial gallbladder motor function: refilling and turnover in health and cholelithiasis. Gastroenterology. 1995;109:582-591.
 20. Kayacetin E, Kisakol G, Kaya A, Akpinar Z. Real time sonography for screening of gallbladder motility in diabetic patients: relation to autonomic and peripheral neuropathy. Neuro Endocrinol Lett. 2003;14:73-76.
 21. Gaur C, Mathur A, Agarwal A. Diabetic autonomic neuropathy causing gallbladder dysfunction. J Assoc Physicians India. 2000;48:603-605.
 22. Hahm JS, Park JY, Park KG, *et al.* Gallbladder motility in diabetes mellitus using real time ultrasonography. Am J Gastroenterol. 1996;91:2391-2394.
 23. Stone BG, Gavalier JS, Belle SH, *et al.* Impairment of gallbladder emptying in diabetes mellitus. Gastroenterology. 1988;95:170-176.
 24. Keshavarzian A, Dunne M, Iber FL. Gallbladder volume and emptying in insulin-requiring male diabetics. Dig Dis Sci. 1987;32:824-828.
 25. DeBoer SY, Masclee AAM, Lam WF, *et al.* Effect of hyperglycaemia on gallbladder motility in type I (insulin-dependent) diabetes mellitus. Diabetologia. 1994;37:75-81.

26. Raman PG, Patel A, Mathew V. Gallbladder disorders and diabetes mellitus type-2. A clinic-based study. *J Assoc Physicians India*. 2001;50:887-890.
27. Stone BH, Gavalier JS, Bell SH, *et al*. Impairment of gallbladder emptying in diabetics mellitus. *Gastroenterology*. 1988;95:170-6.
28. Pazzi P, Scagliarini R, Gamkerini S, *et al*. Review article gallbladder motor function in diabetes mellitus. *Alimentary pharmacology and therapeutics*. 2000;14(S)2:62-65.
29. Yang CC, Sun SS, Lin CC, *et al*. Evidence of impaired gallbladder function in patients with non-insulin dependent diabetes mellitus by quantitative cholescintigraphy. *Journal of Diabetes and its Complications*. 2002;16(5):347-51.
30. Kayacetin E, Kisakol G, Kaya A, *et al*. Real time sonography for screening of gallbladder motility in diabetic patients in relation to autonomic and peripheral neuropathy. *Neuroendocrinology*. 2003;24(1-2):73-76.