



Diabetic Autonomic Neuropathy a Risk Factor for Gall Stone Disease: a 100 Cases Cross Sectional Study in Indian Population

* Dr. Maninder kaur

Senior resident, medicine department, SGRD medical college, flat no 6, A block SGRD campus, Amritsar. * Corresponding author

Dr. Davinder Mahajan

Professor , medicine department SGRD medical college, Amritsar , SGRD campus

Dr. Parminder Virdi

Senior resident, orthopaedic department, SGRD medical college, Amritsar.

ABSTRACT

Aims and objectives: The present study was conducted to evaluate the association of gall stone disease in type 2 diabetic patients in Indian population and to evaluate the correlation of GSD with autonomic neuropathy. **Method and materials:** The study was conducted on randomly selected 100 clinically diagnosed type 2 diabetic patients matched with 100 healthy randomly selected non diabetic patients. Prevalence of gall stone disease was noted with ultrasound evidence of gall stone disease. Patients with and without gall stone disease were further examined for autonomic neuropathy clinically. **Results:** In diabetic population gall stone disease was present in 45 patients and absent in 55 patients and in non-diabetic group gall stone was present in 15 subjects and absent in 85 subjects. In patients having diabetes with gall stone disease, autonomic neuropathy was present in 26 and absent in 19 patients. While in patients having diabetes without gall stone disease ANP was present only in 13 patients and absent in 42 patients. **Conclusion:** Diabetes is a definitive risk factor for gall stone disease and association of autonomic neuropathy with prevalence of gall stone disease is highly significant in our study.

KEYWORDS : Autonomic neuropathy (ANP), Gall stone, Diabetes mellitus.

Introduction:

Diabetes mellitus is one of the risk factors in cholesterol gallstones. Individuals with diabetes mellitus are reported to have a 2-fold to 3-fold increase in the incidence of cholesterol gallstones^[1]. Cholesterol stones account for more than 90 % of gall stone in western industrialized countries. There are several important mechanisms in formation of lithogenic bile, the most important is increased biliary secretion of cholesterol. This may be associated with obesity, metabolic disorder like diabetes, high caloric and cholesterol rich diets or drugs (clofibrate)^[2].

Other important mechanism in cholesterol gall stone formation is gall bladder hypomotility leading to delayed gall bladder emptying and stasis^[3]. Diabetic neuropathy develops in approximately 50% individuals with long standing type 1 and 2 DM. It may manifest as polyneuropathy, mononeuropathy and autonomic neuropathy among which polyneuropathy is most common^[4]. Contractibility of the gallbladder is reduced as a consequence of diabetic neuropathy in diabetics. Such phenomenon reduces the frequency of enter hepatic cycling of the bile salt pool and results therefore in an expansion of both the bile salt pool and biliary cholesterol secretion. Such responses allow cholesterol to accumulate within the gallbladder, in excess of the other solubilizing biliary lipids. In addition, gallbladder distention and stagnation associated with diabetic neuropathy allows such supersaturated bile to precipitate its cholesterol content and the resultant stones to grow^[5].

The present study aimed to find out the association of gallbladder disease in type 2 diabetes mellitus patients and to check whether autonomic neuropathy is a risk factor for GSD in diabetics.

Aims:

1. To study the association of gallstone disease in type 2 diabetes mellitus.
2. Comparison of gall bladder diseases in patients with/without autonomic neuropathy.

Methods and material

The present study was carried out in the Department of medicine, Shri Guru Ram Dass medical college Amritsar. The type 2 diabetic patients were selected at random from outpatient clinics and in-pa-

tient services of the hospital. For the diagnosis and classification of diabetes, ADA criteria of fasting glucose > 126 mg/dl were used. The present study included 100 cases of diabetic Patients in age group 40-70yrs. 100 healthy Non diabetic and matched subjects for age and sex without any previous gall bladder disease comprised the control group.

Ultrasound examination of abdomen was performed after 12 hours of overnight fasting in the morning using real time scanner with 3.5 megahertz transducer. Both cases and control group were assessed with ultrasound. Presence of gall stone and sludge were considered positive for gall stone disease.

The diabetic patients with gall stone disease were further examined for autonomic neuropathy.

Autonomic neuropathy was assessed using non-invasive bedside tests like:

Heart rate response to valsalva manoeuvre

Heart rate variation during deep breathing

Immediate heart rate response to standing

Blood pressure response to standing

Blood pressure response to sustained handgrip

The results of the above mentioned tests were recorded and interpreted according to the Ewing and Clarke criteria^[6].

EWING AN CLARKE CRITERIA

	Normal	Borderline	Abnormal
Test reflecting para sympathetic dysfunction			
Heart Rate Response to Valsalva (Valsalva Ratio)	≥1.21	1.11-1.20	≤1.10
Heart Rate Variation during deep breathing (beats/minute)	≥15	11-14	≤10
Heart Rate Response to standing (0:15 ratio)	≥1.04	1.01-1.03	≤1.00
Test reflecting sympathetic dysfunction			
Blood Pressure response to standing (mmHg)	≤10	11-29	≥30
Blood Pressure response to sustained handgrip (mmHg)	≥16	11-15	≤10

The results were then categorized, and they fell into one of the four groups: normal, early parasympathetic damage with results of one of the three tests of parasympathetic function abnormal, definite parasympathetic damage with results of at least two of the tests of parasympathetic function abnormal, and combined parasympathetic and sympathetic damage, where in addition to abnormal parasympathetic test results findings in on or both of the sympathetic tests were abnormal.

Results :

Table 1.shows that in the study group GSD was present in 45 (45%) of patients and was absent in 55 (55%). In control group GSD was present in 15 (15%) and absent in 85 (85%) which was highly statistically significant with p value <.0001.

45 diabetic patients with gall stone were examined for presence or absence of autonomic neuropathy. Table 2 shows distribution of patients in study group according to ANP. In diabetic patients with gall stone group, ANP was present in 26 (57.7%) patients and absent in 19 (42.2%) patients. In group having diabetes without gall stone disease, ANP was present in 13(23.6%) patients and absent in 42(76.4%). Chi square value was 15.012 and p value was .00001 which was highly significant.

Percentage contraction of various groups is as follows:

DM+ANP+GSD	=	57.7%
DM+ANP-GSD	=	23.6%
DM-ANP+GSD	=	42.2%
DM-ANP-GSD	=	76.4%

Table 1 showing incidence of GSD in study and control group

GSD	Study Group with DM		Control Group	
	No.	%age	No.	%age
Absent	55	55	85	85
Present	45	45	15	15

Statistical analysis

GSD	Chi- square value	p value	Significance
	21.42	<.0001	Highly Significant

Table 2: Incidence of autonomic neuropathy (ANP) in study group only

ANP	GSD +		GSD -	
	No.	%age	No.	%age
Present	26	57.7%	13	23.6%
Absent	19	42.2%	42	76.4%

Statistical Analysis

	Chi- square value	p value	Significance
GSD	15.012	.00001	Highly Significant

Discussion:

The various studies conducted in the past have shown positive correlation between gall stone disease and diabetic mellitus. Our present study too has shown a positive correlation between the GSD and DM. These results are in accordance with study done by Hahm et al (1996)^[1], Várkonyi T1 et al(1997)^[7], Gaur c et al (2000)^[8] and G. Palasciano et al(1992)^[9].It has almost confirmed that there is increased prevalence of gall bladder dysfunction among diabetics causing larger gall bladders with reduced responsiveness to meals which might lead to stasis of bile and development of complications like sludge and cholelithiasis .

Although exact pathophysiologic basis of gall bladder dysfunction in diabetic population is yet not clear, motor abnormalities of gall bladder function is one of the proposed mechanisms. These motor abnor-

malities include large size and impaired contractility of gall bladder due to vagal visceral neuropathy. The similar studies as mentioned above has found significant positive correlation of gall stone disease with autonomic neuropathy^{[11],[7],[8],[9]}. Our study has also found statistically significant correlation between GSD and ANP. Studies done by RS gupta et al^[10] and Stone BG et al (1988)^[11] also showed positive association of GSD with ANP. Other proposed mechanism like impaired release of cholecystokinin or impaired function of cholecystokinin receptors on gall bladder need to be investigated further.

Conclusion

We therefore conclude that diabetes mellitus is a risk factor for gall stone disease. Impaired gall bladder contraction was found amongst patients of diabetes mellitus with autonomic neuropathy. The mechanism responsible for cholecystoparesis is attributed to vagal neuropathy. Incomplete gall bladder emptying leads to sequestration of cholesterol and nidus formation. Therefore gall bladder functions should be evaluated routinely in such patients and early intervention is recommended.

REFERENCES

- Hahm JS1, Park JY, Park KG, Ahn YH, Lee MH, Park KN. Gallbladder motility in diabetes mellitus using real time ultrasonography. Am J Gastroenterol. 1996 Nov; 91(11):2391-4.
- Norton j, Harrison's principles of internal medicine vol 2,19th edition(2015), p.2076-2077.
- Norton j, Harrison's principles of internal medicine vol 2,19th edition(2015), p.2078
- Norton j, Harrison's principles of internal medicine vol 2,19th edition(2015), p.2426.
- Thiel DHV. Diabetes mellitus and hepatobiliary disease. Acta Medica Portuguesa 1984; 5:59-65.
- Ewing DJ and Clark BF. Diagnosis and management of diabetic autonomic neuropathy. Br Med J 1982; 285:916.
- Varkonyi T1, Lengyel C, Madácsy L, Velösy B, Boda K, Kempler P, Fazekas T, Csernay L, Lonovics J. Gallbladder hypo motility in diabetic polyneuropathy Orv Hetil. 1997 May 11; 138(19):1177-82
- Gaur C1, Mathur A, Agarwal A, Verma K, Jain R, Swaroop A. Diabetic autonomic neuropathy causing gall bladder dysfunction. J Assoc Physicians India. 2000 Jun;48(6):603-5.
- G. Palasciano MD1, P. Portincasa1, A. Belfiore1, G. Baldassarre1, M. Cignarrelli2, A. Pater-nostro 2, O. Albano1 and R. Giorgino 2.Gallbladder volume and emptying in diabetics: the role of neuropathy and obesity. Wiley online library journal of internal medicine. DOI: 10.1111/j.1365-2796.1992.tb00512.x.
- RS Gupta, HK Rao, AR Singh, AP Singh .Gall Bladder Disease in Type 2 Diabetes Mellitus. www.japi.org/april2008/Oral_Diabetes%20Mellitus_Endocrinology_Clinical%20Pharmacology.html
- Stone BG1, Gavaler JS, Belle SH, Shreiner DP, Peleman RR, Sarva RP, Yingvorapant N, Van Thiel DH . Impairment of gallbladder emptying in diabetes mellitus. Gastroenterology. 1988 Jul;95(1):170-6.