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Prevalence of Gall-Bladder Disorders in Diabetic Patients with Autonomic Neuropathy

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Abstract: *Introduction:* Type-2 diabetes mellitus are reported to have a 2 to 3-fold increase in the incidence of cholesterol gallstones. Gallstone disease in patients with diabetes mellitus is largely due to dyslipidemia, leading to the alteration in the composition of bile. Impairment of gallbladder motility and contraction, as a result of hyperglycemia and diabetic autonomic neuropathy. Hence the study is undertaken to determine prevalence of gall-bladder disorders in diabetic patients with autonomic neuropathy and association of different parmaetrs with Cases and without autonomic neuropathy. Material & Methods: This was a hospital based case-control study carried out during the period of October 2010 to October 2012. Institutional ethics committee approved the study.The study comprised of known or newly diagnosed 101 patients of type-2 diabetes mellitus and 101 age and sex matched controls. Observation & Results: Out of 101 cases studied 67(66.33%) had autonomic neuropathy and out of 101 controls 9(8.91%) had autonomic neuropathy. Thus prevalence of autonomic neuropathy was significantly more in cases than controls. Out of 67 cases with autonomic neuropathy 32 (47.76%) had gallbladder disorders and out of 34 cases without autonomic neuropathy 4(11.76%) had gallbladder disorders. Thus prevalence of gallbladder disorders in cases with autonomic neuropathy was significantly more than in cases without autonomic neuropathy. Conclusion: Present study concluded that Gallbladder disorders are significantly associated with metabolic syndrome in type-2 diabetics.Type-2 diabetics with autonomic neuropathy have larger gall bladders with poor contraction in response to fatty meals, thus predisposing these patients to various forms of gall bladder disease.

Keywords: Gallbladder Disorders, autonomic neuropathy.

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INTRODUCTION

Diabetes mellitus is a group of metabolic disorders characterized by hyperglycemia resulting from defects in insulin secretion, insulin action or both. The chronic hyperglycemia of diabetes is associated with damage, dysfunction and failure of various organs, especially the eyes, kidneys, nerves, heart and blood vessels [1]. Various studies point towards the increased prevalence of gall bladder diseases like gall stones in diabetics. This has been attributed to cholecystomegaly & impaired gall bladder contraction, mainly due to autonomic neuropathy seen in diabetics [2].

Since the asymptomatic period of hyperglycemia, is on an average of 5 to 7 years, many individuals tend to have complications of diabetes microvascular or macrovascular at the time of diagnosis itself. Among various microvascular complications like retinopathy, nephropathy and neuropathy, autonomic neuropathy although a well recognized complication, has been given less attention. In autonomic neuropathy involvement of both parasympathetic and sympathetic chains leads to various manifestations involving various organs in the body, autonomic manifestations in the gastrointestinal tract includes gastropathies, nocturnal diarrhea, esophageal dysmotility, constipation and gallbladder dysfunction, being consequence of vagal neuropathy leading to reduced gastrointestinal motility.

Individuals with type-2 diabetes mellitus are reported to have a 2 to 3-fold increase in the incidence of cholesterol gallstones. Studies have shown a higher prevalence of gallstone disease in patients with type-2 diabetes mellitus and that type-2 diabetes mellitus is an independent predictor for increased gallbladder volume.

Cholesterol stones are the most common type of gall stones in western population. The risk factors for cholesterol gall stones are; increasing age, female gender, multi-parity, obesity, rapid weight loss, diet (those high in animal fat), drugs

(such as contraceptive pills) and ileal disease or resection. Others are liver cirrhosis, haemoglobinopathy and diabetes mellitus [3].

Females are reported to have an increased risk of gallbladder disorders till the age of 50 probably due to hormonal influence on bile composition and gallbladder motility [4].

Gallstone disease in patients with diabetes mellitus is largely due to dyslipidemia, leading to the alteration in the composition of bile. Impairment of gallbladder motility and contraction, as a result of hyperglycemia and diabetic autonomic neuropathy, also cause bile stasis and promote cholesterol gall stone crystal formation [5].

Individuals with type-2 diabetes mellitus are reported to have a 2 to 3-fold increase in the incidence of cholesterol gallstones. Studies have shown a higher prevalence of gallstone disease in patients with type-2 diabetes mellitus and that type-2 diabetes mellitus is an independent predictor for increased gallbladder volume.

The fasting gallbladder volumes were significantly increased in patients with multiple gallstones and that, diabetic patients with autonomic neuropathy showed a decreased gallbladder emptying rate [5].

Hence the study is undertaken to determine prevalence of gall-bladder disorders in diabetic patients with autonomic neuropathy and association of different parmaetrs with Cases and without autonomic neuropathy.

MATERIALS AND METHODS:

This was a hospital based case-control study carried out during the period of October 2010 to October 2012. Institutional ethics committee approved the study.

The study comprised of known or newly diagnosed 101 patients of type-2 diabetes mellitus, above age of 12 years, attending Medicine OPD or admitted in medicine wards at our hospital and 101 age and sex matched controls, taken from patients coming to Medicine OPD for minor complaints, who were unrelated to diabetic patients and without history/diagnosis of diabetes.

A detailed clinical history was recorded regarding symptoms related to diabetes and symptoms related to gallbladder disorder and autonomic neuropathy (biliary colic, fever, jaundice, flatulence, postmeal epigastric fullness, postural dizziness, constipation, nocturnal diarrhea and gustatory sweating).

Past history of jaundice, fever, abdominal pain, duration of diabetes was recorded. Treatment history of diabetes and family history of diabetes was recorded. Complete clinical examination was done for all consenting subjects including detailed general examination, abdominal examination, respiratory system, cardiovascular system, central nervous system. . Body weight, height, body mass index, waist circumference and hip circumference were recorded. Waist- hip ratio was calculated. Cardiovascular autonomic function tests were performed and findings were recorded.

Hematological investigations were carried out including complete blood count, peripheral smear. Biochemical investigations including ,fasting and 2 hour postprandial plasma glucose levels, glycated hemoglobin (HbA_{1C}), liver function test, lipid profile, serum creatinine, urine albumin were performed.
All the findings were recorded in prescribed proforma. Once basic examination and blood tests were over subjects were taken for ultrasound of abdomen.

Study design: Case Control Study at a Tertiary Care Teaching Institute.
Study Setting – Medicine OPD and Medicine wards Under Department of Medicine.
Inclusion criteria for cases:
Known and newly diagnosed cases of type-2 diabetes mellitus (ADA criteria) more than 12 years of age.
Diabetic patients giving informed consent.

Exclusion criteria for cases:

- Sickle cell disease and other chronic hemolytic disorders.
- Patients having complications of diabetes like diabetic ketoacidosis, hyperglycemic hyperosmolar state.
- Patients having acute myocardial infarction, unstable angina & acute cerebrovascular accidents.
- Previously or recently diagnosed congenital and anatomical anomalies and abnormalities of biliary system.
- Refusal to give informed consent.

Inclusion Criteria for Controls:

- Age group (± 5yrs) and sex matched healthy controls randomly selected from:-
- Healthy attendants and other healthy staff of hospital.
- Healthy subjects who visit the medicine OPD for minor complaints.

Exclusion Criteria for Controls:

- Any evidence of diabetes mellitus.
- Previously or recently diagnosed congenital and anatomical anomalies and abnormalities of biliary system.
- Subjects with hemolytic disorders.
- Those who do not give informed consent.
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Cases of type-2 diabetes mellitus attending medicine OPD and/or admitted in medicine wards who meet the above eligibility criteria were enrolled in the study. Written and informed consents of subjects were taken.

Detailed history about general health, symptoms of gallbladder disorders and autonomic neuropathy was obtained through an interviewer administered questionnaire. Past history about biliary colic, fever, jaundice, duration of diabetes, treatment history of diabetes and family history was recorded. Personal history regarding smoking, alcohol consumption, bowel and bladder habits and drug intake was recorded.

Detailed general and systemic examination including per abdominal respiratory, cardiovascular examination was done. Anthropometric measurements and cardiovascular autonomic function test findings were recorded.

Investigations like fasting and postmeal blood sugar, glycated hemoglobin, Complete Blood Count, Liver function test, lipid profile, urine albumin were done. All the selected subjects underwent ultrasonography of abdomen with special interest for gallbladder.

Statistical Analysis:

Results on continuous measurements were presented as mean ± S.D. and results on categorical measurements were presented in Number (%). For categorical data, Chi square was used and Fischer exact test for small numbers. For continuously distributed variables, students T test and Z test was used. Comparison between multiple groups was done by generalized linear model. 'p' value of 0.05 or less was considered to be statistically significant

Observations & Results:

The present study was carried out at department of medicine at our institute between period of October 2010 to October 2012. We included 101 cases of type-2 diabetes mellitus and 101 age and sex matched healthy controls from the normal population in the study.

After a detailed clinical history and complete clinical examination, anthropometric, cardiovascular autonomic testing and routine hematological and biochemical investigations were carried out and there after ultrasonographic evaluation of gallbladder was done in both cases and controls.

Table 1: Age Distribution Of Cases And Controls

Age Group (years)	Cases (n=101)	Controls (n=101)
40 to 49 years	9(8.91%)	11(10.91%)
50 to 59 years	42(41.58%)	42(41.58%)
60 to 69 years	42(41.58%)	40(39.60%)
70 to 80 years	8(7.92%)	8(7.92%)
TOTAL	101(100%)	101(100%)
Mean age± SD	59.61±6.86	59.51±6.85

In the present study mean age of cases was 59.61±6.86 years and mean age of controls was 59.51±6.85 years. Minimum age in cases was 40 years and maximum age was 75 years. Most of the cases were in the age group of 50 to 59 years (n=42)(41.58%) and in the age group of 60 to 69 years (n=42)(41.58%). There were no cases of type-2 diabetes below age of 40 yrs. and above age of 80 years.

Table 2: Gender Distribution Of Cases And Controls

Gender	Cases (n=101)	Controls (n=101)
Males	47(46.53%)	47(46.53%)
Females	54(53.46%)	54(53.46%)
TOTAL	101(100%)	101(100%)

In our study we included 101 cases with type-2 diabetes and 101 age (±5 years) and sex matched healthy subjects. Out of 101 cases 47 (46.53%) were male and 54 (53.46%) were female. Similarly out of 101 controls 47 (46.53%) were male and 54 (53.46%) were female.

Table 3: Distribution of Autonomic Neuropathy in Cases and Controls

	Cases (N=101)	Controls (N=101)	X2-value	p-value
Number of patients with autonomic neuropathy	67(66.33%)	9(8.91%)	69.31	0.0001*
Number of patients without autonomic neuropathy	34(33.66%)	92(91.08%)		

(* indicates statistically significant at 5% level of significance)

Out of 101 cases studied 67(66.33%) had autonomic neuropathy and out of 101 controls 9(8.91%) had autonomic neuropathy. Thus prevalence of autonomic neuropathy was significantly more in cases than controls.

Table 4: Correlation of Gallbladder Disorders in Cases with Autonomic Neuropathy.

	cases with autonomic neuropathy (n=67)	cases without autonomic neuropathy (n=34)	ϰ2-value	p-value
Cases with gallbladder disorders (N=36)	32 (47.76%)	4 (11.76%)	30.86	0.0001*
Cases without gallbladder disorders (N=65)	35 (52.24%)	30 (88.24%)		

(* indicates statistically significant at 5% level of significance)

In the present study, out of 67 cases with autonomic neuropathy 32 (47.76%) had gallbladder disorders and out of 34 cases without autonomic neuropathy 4(11.76%) had gallbladder disorders. Thus prevalence of gallbladder disorders in cases with autonomic neuropathy was significantly more than in cases without autonomic neuropathy.

Table 5: Correlation of Gallbladder Volumes and Motility In Cases with Autonomic Neuropathy

Sonographic Characteristics Of Gallbladder	Cases With Autonomic Neuropathy (N =67) Mean ± S.D.	Cases Without Autonomic Neuropathy (N =34) Mean ± S.D.	Z-Value	P-Value
Fasting Gallbladder Volume	26.02±2.70cc	23.19 ±2.17cc	5.39	0.000*
Post meal Gallbladder Volume	14.14±1.59cc	11.59 ± 1.96cc	7.06	0.000*
Gallbladder Motility (% contraction)	45.62 ± 4.22%	50.15 ±5.71%	4.53	0.000*

(* indicates statistically significant at 5% level of significance)

In the 101 cases studied, 67 had autonomic neuropathy in whom mean Fasting Gallbladder Volume was 26.02±2.70cc, mean Post meal Gallbladder Volume 14.14±1.59cc, mean gallbladder contraction was 45.62 ± 4.22%. Out of 101 cases 34 were without autonomic neuropathy in whom mean Fasting Gallbladder Volume was 23.19 ±2.17cc , mean Post meal Gallbladder Volume 11.59 ± 1.96 cc , mean gallbladder contraction was 50.15 ±5.71%. The difference in gallbladder volumes and motility in patients with and without autonomic neuropathy was statistically significant ('p' value<0.05).

Table 6: Distribution of Cases according to Presence of Metabolic Syndrome

CASES (N=101)	Males (N=47)	Females (N=54)	Total (n=101)
Cases with metabolic syndrome	21 (20.79%)	20 (19.80%)	41(40.59%)
Cases without metabolic syndrome	26 (25.74%)	34 (33.66%)	60 (59.41%)

+Out of 101 cases studied 41(40.59%) cases had metabolic syndrome, out of which 21(20.79%) were males and 20 (19.80%) were females. 60 (59.41%) cases were without metabolic syndrome.

Table 7 : Correlation of Gallbladder Volumes and Motility in Cases with Presence Of Metabolic Syndrome.

Sonographic Characteristics Of Gallbladder	**Cases with metabolic syndrome (n=41) Mean ± S.D.**	**Cases without metabolic syndrome (n=60) Mean ± S.D.**	**z-value**	**p-value**
Fasting Gallbladder Volume	24.90 ±2.75cc	23.72± 2.64cc	2.154	0.034*
Post meal Gallbladder Volume	13.24±1.81cc	12.01±2.32cc	2.976	0.004*
Gallbladder Motility (% contraction)	46.82±4.70%	49.70±6.00%	2.721	0.008*

(* indicates statistically significant at 5% level of significance)

In the cases with metabolic syndrome mean fasting gallbladder volume was 24.90 ±2.75CC, mean post meal gallbladder volume was 13.24±1.81cc and mean gallbladder contraction 46.82±4.70%. In the cases without metabolic syndrome mean fasting gallbladder volume was 23.72 ±2.64CC, mean post meal gallbladder volume was 12.01±2.32cc and mean gallbladder contraction 49.79±6.00%. The difference in gallbladder motility and volumes in cases with and without metabolic syndrome was statistically significant ('p' value <0.05).

Table 8: Comparison of Clinical Characteristics in Cases with and Without Gallbladder Disorders

Clinical Characteristics	**Cases with gallbladder disorders (n=36)**	**Cases without gallbladder disorders (n=65)**	**z-value**	**p-value**
Age	61.5 ± 7.23yr.s	58.56 ± 6.48yr.s	2.08	0.0387*
Male: Female Ratio	7:11	33:32	0.79	0.37
Number of cases with metabolic syndrome	18 (50%)	23 (35.38%)	10.76	0.001*
Number of cases with autonomic neuropathy	32 (88.89%)	35 (53.85%)	30.06	<0.000*

(* indicates statistically significant at 5% level of significance)

The mean age in cases with gallbladder disorders was 61.5 ± 7.232 and in cases without gallbladder disorders was 58.56 ± 6.48, difference in them was statistically significant (p<0.05). The difference in male to female ratio in patients with and without gallbladder disorders was not significant.

The number of cases with metabolic syndrome in cases with gallbladder disorders was 18 (50%) and in cases without gallbladder disorders was 23 (35.38%). The difference in them was statistically significant (p value<0.05). The number of cases with autonomic neuropathy in cases with gallbladder disorders was 32 (88.89%) and in cases without gallbladder disorders was 35 (53.85%). The difference in them was statistically significant (p value<0.05).

Table 9 : Correlation of Gallbladder Volumes and Motility in Cases with Gallbladder Disorders

	Cases with gallbladder disorders (n=36) Mean ± S.D.	**Cases without gallbladder disorders (n=65) Mean ± S.D.**	**z-value**	**p-value**
Fasting Gallbladder Volume	26.02± 2.71cc	23.19± 2.17cc	5.39	0.000*
Postmeal Gallbladder Volume	14.15 ± 1.59cc	11.59 ± 1.96cc	7.06	0.000*

Gallbladder Motility (% contraction)	45.62 ± 4.22%	50.15± 5.71%	4.53	0.000*

(* indicates statistically significant at 5% level of significance)

In the cases with gallbladder disorders mean fasting gallbladder volume was 26.02± 2.71cc, mean post meal gallbladder volume was 14.15 ± 1.59cc, mean gallbladder contraction was 45.62 ± 4.22%. In the cases without gallbladder disorders mean fasting gallbladder volume was 23.19± 2.17cc, mean post meal gallbladder volume was 11.59 ± 1.96, mean gallbladder contraction was 50.15± 5.71%. The difference in gallbladder volumes and motility in cases with and without gallbladder disorders was statistically significant ('p' value<0.05).

Table 10: Distribution of Cases With Hba_{1c} Level

	HbA_{1C} LEVEL <7%	**HbA_{1C} LEVEL ≥7%**
Males (N=47)	8 (17.02%)	39 (82.98%)
Females (N=54)	15 (27.78%)	39 (72.22%)
Total (N=101)	23 (22.78%)	78 (77.22%)

Out of 101 cases 23(22.78%) had HbA_{1C} level <7%, of these 8 (17.02%) were males and 15 (27.78%) were females. 78 (77.22%) had HbA_{1C} level ≥7% of these 39 (82.98%) were males and 39 (72.22%) were females. (HbA_{1C} level of 7% is target level of diabetes control).

Table 11: Distribution Of Gallbladder Volumes And Motility With Hba_{1c} Level

	Cases With HbA_{1C} Level <7% (N=23) Mean ± S.D.	**Cases With HbA_{1C} Level ≥ 7% (N=78) Mean ± S.D.**	**z-value**	**p-value**
Fasting Gallbladder Volume	23.45 ± 2.64cc	24.42 ± 2.73cc	1.53	0.133
Postmeal Gallbladder Volume	11.85 ± 2.01cc	12.7 ± 2.23cc	1.73	0.091
Gallbladder Motility (% contraction)	49.68 ± 5.15%	48.20 ± 5.77%	1.17	0.248

(* indicates statistically significant at 5% level of significance)

In the cases with HBA1C level<7% , mean fasting gallbladder volume was 23.45 ± 2.64cc , mean post meal gallbladder volume was 11.85 ± 2.01cc and mean gallbladder contraction was 49.68 ± 5.15%. In the cases with HBA1C level>7% , mean fasting gallbladder volume was 24.42 ± 2.73 , mean post meal gallbladder volume was 12.7 ± 2.23cc and mean gallbladder contraction was 48.20 ± 5.77%. The difference in gallbladder volumes and motility in these two groups was not statistically significant. ('p' value >0.05).

DISCUSSION:

In present study mean duration of diabetes was significantly more in cases with gallbladder disorders. Similar results were found in study conducted by PG Raman *et al.,* [4], i.e. the mean duration of diabetes in diabetics with gallbladder disorders was (6.9±5.1) significantly more than in diabetics without gallbladder disorders. Also Haffner *et al.,* [6] documented a positive correlation of gallbladder disorders with duration of diabetes. But in the study conducted by Elmehdawi RR *et al.,* [7] significant correlation was not found. S Singh *et al.,* [8] it was found that duration of diabetes mellitus is positively related to prevalence of gallbladder disease. The mean duration of diabetes in patients with autonomic neuropathy was 13.6 years and in diabetics without autonomic neuropathy was 6.04 years. Thus autonomic neuropathy becomes more prevalent with increasing duration of diabetes, leading to increase in prevalence of gallbladder disorders in cases with diabetes [8].

The difference in gallbladder volumes among cases with different duration of diabetes was found to be significant ('p' value<0.05) i.e. larger fasting gallbladder volumes were found in cases with longer duration of diabetes. Similar findings were observed in the study conducted by Sefa Guliter *et al.,* [9] in which fasting gallbladder volume and duration of diabetes mellitus showed significant correlation (r = 0.212; $P < 0.05$). Decreased gallbladder motility was observed in cases with longer duration of diabetes; In the present study comparison of gallbladder motility was done between groups of cases with different duration of diabetes and difference in gallbladder motility found was significant (f =11.25, 'p'<0.05). No study was found in which such comparison was done. Longer the duration of diabetes, more chances of developing complications like autonomic neuropathy and leading to decreased gallbladder motility and biliary stasis and gallbladder disorders [4].

In the present study significantly high percentage of cases (47.76%) with autonomic neuropathy had gallbladder disorders than cases without autonomic neuropathy (11.76%) ('p' value <0.05). Similar results were found in the study conducted by S Singh *et al.,* [8] Gall bladder emptying was found to be impaired more among diabetics having autonomic neuropathy and autonomic neuropathy promotes the biliary stasis and gallstone formation [4]. Thus, we suggest that impairment of gallbladder motility complicated with autonomic neuropathy causes stasis and results in cholesterol gallstone crystal formation and gallstone growth [10].

In the present study significant difference was found in fasting gallbladder volume in the cases with (26.02±2.70cc) and without (23.19 ±2.17cc) autonomic neuropathy. Similar results were found in the studies conducted by S Singh *et al.,* [8] and PG Raman *et al.,* [4]. In the present study postmeal gallbladder volume was also significantly increased in cases with autonomic neuropathy but no such comparison was made in other studies, but different studies such as S Singh *et al.,* [8] and Palasciano G *et al.,* [11] show decreased postmeal emptying of gallbladder in cases with autonomic neuropathy thus will lead to larger post meal gallbladder volume in them.

In the present study significant difference was found in the mean gallbladder contraction in cases with and without autonomic neuropathy, i.e. gallbladder motility was less in cases with autonomic neuropathy. Similarly in the study conducted by Hahm JS, *et al.,* [5] in diabetics with autonomic neuropathy, gallbladder motility was markedly reduced in comparison to diabetics without autonomic neuropathy. But in the studies conducted by PG Raman *et al.,* [4], S Singh *et al.,* [8], no significant difference was found. Diabetics with autonomic neuropathy tend to have larger gall bladders with poor contraction in response to fatty meals (due to vagal neuropathy), thus predisposing these patients to various forms of gall bladder disease [8].

In the present study prevalence of metabolic syndrome was 50% in cases with gallbladder disorders and 35.38% in cases without gallbladder disorders and the difference was significant ('p' value<0.05). Similar results were found in the study conducted by Nahum Méndez-Sánchez *et al.,* [12] to establish an association between the presence of metabolic syndrome and the development of gallstone disease, and in the study conducted by Li-Ying Chen *et al.,* [13] to investigate the association between metabolic syndrome and the development of gallstone disease.

In the present study both mean fasting (24.90 ±2.75cc) and post meal (13.24±1.81cc) gallbladder volume were significantly higher in cases with metabolic syndrome than in cases without metabolic syndrome (mean fasting gallbladder volume =23.72±2.64cc) (mean postmeal gallbladder volume =12.01±2.32cc).('p' value<0.05). Mean gallbladder motility was significantly less in patients with metabolic syndrome (46.82±4.70%) than in cases without metabolic syndrome (49.70±6.00%).

No study could be found comparing gallbladder motility with metabolic syndrome however in the study conducted by AK Agarwal *et al.,* [14] , gallbladder enlargement in type-2 diabetics , was significantly correlated with body mass index (p<0.01). In female type 2 diabetics, gallbladder volume was significantly correlated with waist-hip ratio (p<0.01). In male type 2 diabetics, gallbladder volume was significantly correlated with LDL cholesterol levels (p <0.05).

In the present study no significant difference ('p' value>0.05) was found in gallbladder volumes and motility in cases with HbA_{1C}<7% and HbA_{1C} ≥7% a (HbA_{1C} level of 7% is target level diabetes control[1].) Similar results were found in the study conducted by AK Agarwal *et al.,* [14], who found no significant correlation between fasting gallbladder volume and HbA_{1C} level. However, no study was found which compares gallbladder motility with HbA_{1C} level. In the present study mean fasting gallbladder volume was significantly larger in cases with gallbladder disorders than cases without gallbladder disorders similar results were obtained in the study conducted by PG Raman *et al.,* [4]. In the present study mean post meal gallbladder volume was also significantly larger in cases with gallbladder disorders than in cases without gallbladder disorders. Similar findings were reported by the study conducted by Chhabra A *et al.,* [15] in which both fasting and postmeal gallbladder volume were more in cases with gallbladder disorders than in cases without gallbladder disorders.

In the present study mean gallbladder motility was significantly lower in cases with gallbladder disorders than in cases without gallbladder disorders. Similar results were found in the study conducted by PG Raman *et al.,* [4] and Chhabra A *et al.,* [15], Gaur *et al.,* [16], Also according to Stone *et al.,* [17] gallbladder emptying was lower in diabetics with gallbladder disease. The motility defects of gallstone patients are manifested by increased fasting volume, decreased ejection fraction, decreased rate of ejection, and increased residual volume of the gall bladder [14]. Sefa Gu¨liter *et al.,* [18] reported that, although impaired gallbladder emptying was shown in patients with gallstones.

CONCLUSION:

Present study concluded that Gallbladder disorders are significantly associated with metabolic syndrome in type-2 diabetics.Type-2 diabetics with autonomic neuropathy have larger gall bladders with poor contraction in response to fatty meals, thus predisposing these patients to various forms of gall bladder disease.There is no significant correlation of gall bladder disorders with glycemic control.

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