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Gall Bladder Motility Study Evaluation of Asymptomatic Gall Bladder Stones

KEYWORDS: Motility studies, cholelithiasis, asymptomatic gall stone

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ABSTRACT *Aim: To evaluate the validity of gall bladder motility study as a surrogate of GB functional abnormality in patients with incidental asymptomatic gall bladder stone. Asymptomatic cholelithiasis raise significant concern and it is vital to evaluate evidences for elective surgical management. Further, the evidences from existing body of literature are correlated with findings of this study to suggest a possible role of this useful technique.*

Methods: Gall bladder motility study was carried out by ultrasound screening after ingestion of test meal in 54 consecutive cases of asymptomatic gall bladder diseases and in 18 healthy volunteers in our tertiary care center based in a busy university hospital.

Results: 61.1% of cases were poor contractors as compared to 11.1% of controls. The fasting volume of GB in cases, was significantly higher ($p < 0.04$) than in controls. The PP1,PP2 and PP3 were significantly higher in cases of good contractors group as compared to the controls, the volumes being also higher in cases of poor contractors group. The EV was significantly low in poor contractors with a consequent significantly higher RF than the good contractors. The residual fraction was significantly higher in cases as compared to controls ($p<0.02$)

Conclusion: Gall bladder motility study metrics are viable imaging markers for GB functional compromise. The variables evaluated hitherto are independent predictors of GB function. Evidences from contemporary and historically important literature, point towards a direct role of gall bladder stone in causation of complications. It is therefore hypothesized, that elective surgery based on patient selection in accordance with the parameters calculated hereby, can lead to a statistically significant reduction in complication caused by an asymptomatic gall stones.

RUNNING TITLE

Early detection of asymptomatic gall bladder stones can lead to a reduction in complications of calculus cholecystitis. / prediction / potential for formation of stones by gall bladder motility studies

INTRODUCTION

The incidence of asymptomatic gall bladder diseases has been found to range from 8% to 74% [1, 2, 3, 4] depending on the age, ethnicity and co-morbidities. These consist of a heterogeneous group of diseases, the most common being gall stones, carcinoma gall bladder (CaGB), adenomyosis and cholecystitis [1]. The above are diagnosed while sonographic screening of abdomen for unrelated causes, by presence of well defined imaging criteria and appearances established in the literature. Presence of more than one such condition in a patient is not uncommonly seen, and a direct cause effect relationship has been proposed between gall stone and CaGB [5]. Not all cases harboring a gall stone however develop CaGB, hence there seems to be an 'unknown' independent determinant for genesis of both these conditions. Impaired gall bladder motility is one such factor which has been shown to be associated with not only cholelithiasis and Carcinoma GB, but with a multitude of gall bladder diseases [6, 7, 8]. The present study aims at evaluating a possible role of impaired gall bladder motility as an independent causative factor for development of gall stones. This exercise is an attempt towards crystallization of guidelines for timely management of asymptomatic gall stones, otherwise both of which have a potential for causing grave complications [9, 10, 11].

PATIENTS AND METHODS

The presented data set was prospectively gathered over a period of two years at the Radiodiagnosis & surgical unit of our tertiary care and referral center, based at a busy university hospital.

SELECTION OF CASES

Fifty four cases and 18 controls were evaluated in the present study. The cases were consecutively selected from those being referred for sonographic evaluation of an unrelated abdominal condition (Table 1), and in whom detection of a gall bladder stones was purely incidental. The 18 males and 36 females were included with maximum number of female population noted in the age group of 41 – 50 years while most men belong to 21-30 years age group (Table 2). Informed consent was taken from each patient. The study was approved by the institute human ethics committee and review borad.

The controls were randomly selected from healthy volunteers (attendants of patients) who gave informed consent for the same.

METHODS

Ultrasonographic examination of the abdomen was

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performed during evaluation of the primary disease. Incidental gall stones were evaluated with standard B-Mode sonography equipment (Sonoline G50S; Siemens Health systems, Erlangen, Germany), using a 3.5 Mhz convex array transducer.

Volumetric assessment of G.B was done using inbuilt software based on the Simpson's rule of integration for determination of volume, which utilizes the maximum cross sectional area and maximum longitudinal dimension for the purpose (4,7). Three plane imaging of the organ was performed (true transverse & longitudinal, showing maximum dimensions) on a dual screen mode for the purpose of measurements. Gall bladder outline was traced using a free hand cursor in the transverse plane to get the maximum cross sectional area, while the maximum supero-inferior dimension was measured in the longitudinal view (Fig. 1).

Repeat sonography with overnight fasting was done for assessment of gall bladder motility. A baseline measurement of G.B volume (FV) was made following with a test meal comprising of groundnut (75 gm), glucose powder (50 gm), bread and butter (100 gm). The test meal simulated a physiological normal diet as per Indian food table. Subsequent measurements were made at post prandial 30 (PP_1), 60 (PP_2) and 90 (PP_3) minutes following the test meal.

DATA ANALYSIS

The residual fraction (RF) was calculated as the ratio of smallest post-prandial residual volume (RV_X) and fasting volume (FV) [RV_X/FV]. The total ejection volume, which represents maximum possible ejection achieved after a test meal, was estimated as the difference between FV and RV_X i.e FV- RV_X. The cases were qualitatively divided into 'good' and 'poor' contractors, based on the cut-off point of 50% emptying achieved during repeat scanning at 90 minutes. Quantitative assessments were based on ejection fraction (EF) estimates, with those having EF of less than 40 % being considered as 'poor contractors'.

Mean and standard deviations of all assessed volumes (FV, PP1, PP2, PP3 and EV) was calculated for both the cases and controls to achieve stratification between 'Good' and 'Poor' contractors. A direct comparison between the standardized temporal volumes, calculated hitherto, was done to bring out the significance of each individually and in combination with the ejection fraction. The pooled mean was also calculated in each group to demonstrate the overall significance of parameters.

RESULTS

Poor contractility was noted in 61.1% (n=33/54) cases as compared to 11.1% (n=2/18) in the control group. GB contractility was good (good contractors) in 38.8% (n=21/54) cases while most of the controls (n=16/18; 88.9%) were good contractors. The pooled mean of fasting volumes of GB in cases were significantly higher ($p < 0.016$) than that in the controls. Significance of difference was also noted between 'good contractors' in both the case as well as control groups ($p < 0.0397$) while the significance of difference between 'poor contractors' in the case versus control group was minimal ($p=0.466$). The PP1,PP2 and PP3 were significantly higher in cases of good contractors group as compared to the controls ($p < 0.122$; $p < 0.065$; $p < 0.0965$ respectively). Significance could only be attached to the post-prandial volume at 90 minutes (PP3) in cases of poor contractors group as compared to that in controls ($p<0.369$) while PP1 and PP2 remained insignificant ($p<0.507$ and $p<0.591$ respectively). The difference in EV between 'good contractors' of cases versus control groups was not significant ($p<0.328$). No significant difference could however be noted between the ejection volumes of 'poor contractors' ($p<0.914$) and also between the pooled ejection volumes ($p<0.866$). The residual fraction was significantly higher in cases as compared to controls in both the groups as well as when the pooled mean was evaluated ($p<0.0014$, 0.0001 respectively) (Table 4). Notably the significance of difference was maximum for residual fraction followed by PP3 as compared to other variables.

DISCUSSION

Altered gall bladder motility has been considered to be an important factor in causation of gall stones (12, 13). Cholecystokinin (CCK) mediated cholinergic response in the smooth muscle cells of gall bladder wall is the principal factor responsible for normal gall bladder motility (18, 19). Increased density of intrinsic cholinergic neurons has been shown in the GB wall (20).Inflammatory response in the gallbladder wall preceding cholecystitis leads to destruction of these neurons, causing a decrease in gallbladder motility. This may be detected by gall bladder motility studies, much before appearance of obvious wall thickening (14, 20). Similar features were noted in the controls who had poor GB motility. This would further emphasize the role of sonographically demonstrable poor GB contraction in causation of attendant complications. We suggest that cholecystectomy should routinely be offered to all poor contractors.

Large baseline gall bladder volume may be considered as an independent predictor of billiary stasis and the formation of billiary sludge (14). The fact has been based on the data generated from both human and animal studies indicating the presence of altered gall bladder motility even after dissolution of gall stones by bile acid therapy or extracorporeal shock wave lithotripsy (15). In the current study, a significantly large FV was noted in cases with gall stones, with a significant difference in FV between 'good contractors' cases and controls. Only minimal significance could be attached to the difference between the FV in 'poor contractors' cases versus controls. This may be explained by the fact, that ultimately it is the composition of bile and the propensity in an individual for precipitation of bile salts, which are the key factors in gall stone formation (16). Reduction in gall bladder contractility, as indicated in the data, would however be indirectly responsible for an increased interprandial residue in GB, which would serve as a predisposing factor for bile salt precipitation (17). Notable was a statistically significant correlation of gall bladder FV with ejection and postprandial residual volume in cases with cholelithiasis (Table 4).However gall bladder fasting volume, in isolation, does not appear to have a significant bearing on surgical decision making.

The residual fraction (RF) in cases with cholelithiasis, in our dataset, correlated positively with all the three post-prandial volumes (but with varying magnitudes). It should also be noted that significance of difference is maximum in the 90 minutes post-prandial volume (PP3) but similar trends are also reflected in the FV and PP1, suggesting that a PP3 in isolation can serve as a determinant of the fraction of bile retained in the gall bladder. Various studies have emphasized the alteration of GB motility as a function of GB evacuation rate (20, 21,22), the role of sonographic motility screening has not been suggested as yet. Though the correlation of serial measurements with the RF is heterogeneous, it is more consistent when only PP1 and PP3 are considered. Hence, we propose acquisition of at least two measurements (PP30 and PP90) during routine motility evaluation to avoid skewing the result towards either group. The residual fraction was significantly higher and EV was significantly lower in poor contractors with gall stones, suggesting definite billiary stasis when compared with good contractors. The PP1 in our patient group was in the range of 27.32 ± 25.2 to 15.20 ± 3.96 for the poor contractors group while it was between 14.34 ± 10.3 and 09.83 ± 5.51 in the good contractors group. We propose the use of a combination of PP1 of 14 ml $\pm$ 10 ml and EV of 8 ml as a cut-off for surgical option versus conservative observation.

In the present series poor contraction of gall bladder was seen in 61.1% of cases with asymptomatic gall stones. This higher incidence in our study may be either due to

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geographical variation or due to increased incidence of gall stone disease in this region. Pauletzki et al (32, 33) reported elevated fasting volume in cases with cholelithiasis. We have found statistically significant correlation of gall bladder fasting volume with postprandial residual ejection volume in cases with asymptomatic gall stones. Similar correlation was observed by pauletzki et al suggesting that fasting volume maybe an essential factor of gall bladder motility affecting postprandial emptying. These findings are however paradoxical to those by de-chuan chan (23), who found a hypermotile GB in cases having dyspepsia but no other symptoms pertaining to gall stone. As also explained by the group this difference is primarily due to presence of dyspepsia and could be due to associated altered gut motility.

Normal and low EF values are reproducible in long-term studies. Once the EF reaches a low value, it does not return to normal, and a normal value requires many years to become abnormal, both in calculus and acalculus groups (28). The lower limits of normality for gallbladder ejection fraction have been found to be between 30% and 40% by using slower infusions of sincalide. This value however could not be reproduced with the short infusion methods (29,30,31). We found the ejection fractions (as calculated from the ration of EV to FV) to be in the range of 53.6% to 73.2% in good contractors group while 25.9% to 37.9% in poor contractors group. Our results however cannot be directly compared with previous workers as we used a physiological fatty meals based on the dietary patterns in the sub-continent. Based on this data we infer that any fraction below 50% after ingestion of fatty meal places the patient in a high risk group for potential development of complications, as this leads to prolonged pooling of bile in the lumen with increased contact time and inflammation as already discussed. This may be used as a cut-off for offering the surgical option to the patient.

Finally however it must be discussed that any preventive surgical option would definitely depend on a trade-off between relative risk of expectant management versus surgical hazards and logistical issues for individual patients (24,25,26).

CONCLUSION

With increasing number of cholecystectomies advised and performed for asymptomatic gall bladder diseases, it appears to be of prime importance to accumulate evidences for logical management of such conditions. Due to lack of such an evidence based approach, in the present scenario, the protocol is governed by individual clinical situations and surgeon preferences.

Though a powerful research tool, the role of gall bladder motility studies has been constantly under scrutiny in clinical practice, due to non-standardized methodology and lack of objective parameters that can be used to stratify various patient sub-groups and in identifying patients likely to benefit from cholecystectomy. The role of this modality has been evaluated for identification of patients at risk of recurrence following gallstone dissolution with medical therapy, for identification of obese patients at risk of gallstone formation during rapid weight loss and for patients with recurrent biliary colic and acalcolous gallbladder disease (27). Though a low inherent value of measurement of gallbladder motility has been suggested by previous workers in clinical practice (27), the observations in this study favor the role of sonographic motility study in early detection of cases having potential for formation of asymptomatic gall stones, which cannot uncommonly lead to complications. We would further like to emphasize the utility of cholecystectomy in preventing the above mentioned complications in those having poor gall bladder motility.

Table 1. Presenting symptomatology and diagnoses in patient (n=54)

PRESENTING SYMPTOMS	FINAL DIAGNOSIS	NUMBER OF CASES
Bleeding per Vaginum	Uterine myoma / D.U.B	7
Fever	Viral Fever	8
Lower abdominal cramps	Gastroenteritis	12
Secondary infertility - female	Gential tuberculosis/ infections	7
Secondary infertility - male	Azoospermia/chronic infections	9
Abdominal lump	Bowel/renal malignancies	5
Abdominal colic	Appendicitis/ ureteric colic	6

Table 2. Patient (n=54) and control (n=18) demographics

AGE(years)	CASES		CONTROLS	
	MALE	FEMALE	MALE	FEMALE
11-20	1	0	1	1
21-30	8	3	2	2
31-40	5	8	2	2
41-50	2	20	2	2
51-60	1	3	1	1
61-70	1	2	1	1

Table 3. Summary of Gall bladder contractility in Patient (n=54) and control (n=18)

	GOOD CONTRACTORS (A)	POOR CONTRACTORS (B)	p-VALUE (A-B)	RESIDUAL FRACTION (RF)
CASES (1)	38.8% (n=21/54)	61.1% (n=33/54)	0.02	00.63±0.20
CONTROLS (2)	88.9% (n=16/18)	11.1% (n=2/18)	< 0.001	00.32±0.36
p-VALUE (1-2)	0.001	0.001	-	-

Table 4. Gall Bladder pattern after meal in cases with asymptomatic gall stone

GB VOLUME (IN ML)	CASES			CONTROLS			p-VALUE		
	GOOD CONTRACTORS (N=21) [1]	POOR CONTRACTORS (N=33) [2]	TOTAL (N=54) [3]	GOOD CONTRACTORS (N=16) [4]	POOR CONTRACTORS (N=2) [5]	TOTAL (N=18) [6]	(1-4)	(2-5)	(3-6)
FV	30.46±20.1	32.78±24.01	31.87±22.95	17.24±15.5	20.05±8.69	17.55±15.16	0.0397	0.466	0.016
PP1	14.34±10.3	27.32±25.2	22.27±21.67	09.83±5.51	15.20±3.96	10.43±7.54	0.122	0.507	0.026
PP2	14.11±16.7	24.28±21.9	20.32±20.64	5.91±4.60	15.75±6.85	7.00±10.89	0.065	0.591	0.011
PP3	14.23±17.0	26.46±21.5	21.70±20.75	6.85±3.2	12.40±5.30	7.47±6.50	0.0965	0.369	0.006
EV	16.35±14.3	08.50±10.9	11.55±12.91	12.65±4.70	7.65±3.32	12.09±6.73	0.328	0.914	0.866
RF	00.46±0.16	00.74±0.14	00.63±0.20	00.28±0.15	00.62±0.01	00.32±0.36	0.0014	0.241	0.0001

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FV= fasting volume
PP1=post prandial volume at 30 minutes
PP2= post prandial volume at 60 minutes
PP3= post prandial volume at 90 minutes
Residual fraction= ratio of smallest post-prandial residual volume (RV_x) and fasting volume

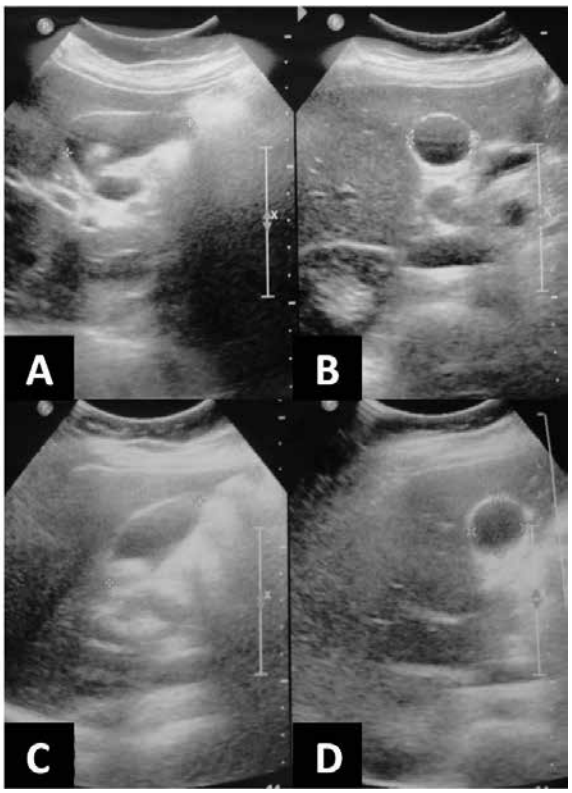

Fig. 1: Longitudinal (A) and Transverse (B) scans with the ultrasound transducer positioned over the right hypochondrium, just below the costal margin, with the patients in right anterior oblique position. The measurements were made in end-inspiration breath hold with 6 hours of fasting. The maximum supero-inferior dimension of the cavity was assessed in longitudinal scan, excluding the wall (A), while the area was measured using the electronic ellipse in the transverse scan (B). The volume was assessed using the automated algorithm installed in the equipment (as described in the text). (C,D) Post-test meal evaluation at 30 minutes (PP1) showing reduction in GB volume.

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