

Original Research Article

Epidemiology, diagnosis and management of patients with biliary dyskinesia and sphincter of Oddi dysfunction: a survey of Indian gastroenterologists

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ABSTRACT

Background: A cross-sectional, physician-based survey was conducted to address the relative lack of data on the awareness about and management of biliary dyskinesia and sphincter of Oddi dysfunction among Indian gastroenterologists.

Methods: A structured questionnaire containing questions on epidemiology, etiology, clinical presentation, diagnostic investigations, prognosis and management was used. Physician responses were analyzed as descriptive statistics and reported as frequency and percentages.

Results: A total 146 gastroenterologists across 137 cities participated in the survey. Majority (76.0%) of physicians stated that <10% of their patients with cholecystitis get diagnosed with BD, while 84.7% stated that <25% of patients with BD have SOD. SOD and BD were reported to be common in females <50 years. Patients recovering from major surgeries/stroke/heart attack/sepsis/extensive trauma were identified by 53.0% of physicians to be at risk for BD. Majority of physicians (69.4%) reported that irritable bowel syndrome (IBS) was a major risk factor for SOD. Cholescintigraphy and hepatobiliary scintigraphy were investigations of choice for BD and SOD according to 55.5% and 33.6% of physicians, respectively. Sepsis was identified as a frequent complication of BD (45.2%). Laparoscopic cholecystectomy was identified by 64.4% participants to result in partial resolution of symptoms in many patients. Calcium channel blockers and antispasmodics were preferred by 55.9% and 30.8% physicians for functional gall bladder disorder, respectively. IBS was the most common indication for prescribing the antispasmodic pinaverium, with the primary objective of pain relief.

Conclusions: Findings from this survey provide insights for further research on BD and SOD in India.

Keywords: Functional gall bladder disorder, Sphincter of Oddi dysfunction, Cholecystectomy, Epidemiology, Treatment of biliary dyskinesia

INTRODUCTION

Biliary dyskinesia (BD) is a functional disorder characterized by biliary pain in the absence of any abnormality in anatomical structure, ultrasound imaging or laboratory parameters. Because of functional nature, the

diagnosis of BD is mainly based on clinical symptoms.¹ Sphincter of Oddi dysfunction (SOD) is another rare disorder that presents with biliary colic and may result from different type of dysfunctions such as spasms, strictures, or inappropriate relaxation.² The rarity of both BD and SOD makes these disorders of exclusion. SOD

affects middle aged females more commonly, and its prevalence is nearly 1.5%. It likely to be an underestimate because of undertesting and lack of concrete biochemical markers for disease diagnosis.³ In patients with suspected biliary pain, quantitative cholescintigraphy and Sostre score criteria can help diagnose BD and SOD.⁴ Manometry is most important diagnostic method for SOD.⁵ However, there are diagnostic challenges especially in resource limited settings. Management of BD largely relies on laparoscopic cholecystectomy with limited options in medical treatment.¹ Cholecystectomy in properly selected patients can provide symptom relief.⁶ Spasmolytic agents; calcium channel blockers (CCBs) and nitrates are considered as initial treatments for SOD and total division of sphincter of Oddi remains the most effective therapy.^{7,8} In India, limited evidence exists pertaining to the understanding of epidemiology, risk factors, diagnostic approach, and management of BD and SOD. This cross-sectional survey among gastroenterologists across India illustrated current practices in India in terms of diagnosis and management of BD and SOD and also identified practices related to the use of the spasmolytic drug pinaverium.

METHODS

Design and settings

This was a cross-sectional, single-point, market research survey that was carried out among gastroenterologists across India to understand the current practices related to BD and SOD. Current treatment approaches for these biliary disorders were also evaluated. The survey was conducted according to the ethical principles of Declaration of Helsinki and applicable national guidelines. We obtained informed consent from each participating physician before survey participation. Ethics committee approval was not obtained as this survey did not constitute direct intervention to patients.

Survey questionnaire

The survey questionnaire included questions pertaining to the epidemiology, etiology, clinical presentation, diagnostic investigations, prognosis and management of BD and SOD (Table 1). Each participating physician provided their response for each of the question in the survey form. The epidemiological questions were pertaining to the prevalence of BD and the age/gender of patients commonly presenting with these disorders. The etiological questions were pertaining to risk factors, setting of common diagnosis, and association of obesity and alcoholism. The clinical presentation questions evaluated the symptoms, differential diagnosis, association with other motility disorders and type of SOD commonly observed in the clinical setting. Questions in the investigations section of the survey form determined the commonly used investigative measures for diagnosis of BD and SOD. Prognostic assessment questions included

failure rates for treatment modalities and use of surgical approach as well as role of pinaverium in BD.

Data collection and analysis

Responses from the physicians were captured in a systematic way and data were entered into Microsoft excel sheet. Data entry was scrutinized for completeness and accuracy by two independent survey team members. After appreciation of accuracy and quality data captured, data were analyzed as descriptive statistics using Microsoft Excel version 2019. Quantitative variables were presented as numbers and frequencies.

RESULTS

Prevalence and risk factors of BD and SOD in Indian clinical practice

A total 146 gastroenterologists across 137 cities from India participated in the survey. According to 76% of the participating physicians, <10% of patients with cholecystitis in their clinical practice get diagnosed with BD, while 84.7% of physicians stated that <25% of their patients with BD have SOD (Table 2). With respect to patient age and gender, 64.3% and 67.5% of participants mentioned that SOD and BD is common in females <50 years, respectively. Type III was the most common type of SOD as identified by 45.5% of physicians, whereas 20.0% and 17.9% reported type I and type II were common types of SOD, respectively (Table 2). According to 53.0% of physicians, the most common risk factor in patients with BD was recovery from major surgeries/stroke/heart attack/sepsis/extensive trauma, whereas long periods of fasting/total parenteral nutrition and drastic weight loss were identified as common risk factors by 43.5% and 24.3% of physicians, respectively (Table 3). Just over half the physicians (54.1%) stated that BD is most commonly seen in ambulatory patients visiting the outpatient department, whereas 29.6% physicians opined that BD occurs in the hospital setting among patients recovering from major surgery/illness. Obesity was observed in very few patients with BD according to majority of the physicians (63.0%). SOD was found to develop after cholecystectomy in <10% of patients according to 68.3% of physicians. Majority of the physicians (69.4%) reported irritable bowel syndrome (IBS) as a major risk factor associated with SOD, followed by preoperative cholelithiasis/gallstone lithotripsy (24.3%; Table 3).

Clinical presentation of comorbidities and complications associated with BD and SOD

The most common presenting symptom in patients with BD was pain in right upper abdominal quadrant and epigastrium according to 89.0% of participants, while bloating (12.3%) and dyspepsia/nausea (17.1%) were less common (Table 4). The most common condition mimicking BD was reported to be cholelithiasis/cholecystitis by 74.0% of the physicians. Differential

diagnosis for BD presenting with typical right upper quadrant abdominal pain was functional dyspepsia (FD)

according to 50.7% physicians, followed by IBS (26.0%), and gastroesophageal reflux disease (4.1%; Table 4).

Table 1: Survey questionnaire.

Questions	
Section 1: Epidemiology of BD	
Q1	How frequently would you estimate that your patients with cholecystitis get diagnosed with BD? a) <10% b) 11%-20% c) 21%-30% d) >31%
Q2	What percentage of your patients with BD are found to be associated with SOD? a) <25% b) 26%-50% c) 51%-75% d) >75%
Q3	In what gender do you see SOD and BD more commonly? a) Females <50 years b) Males <50 years c) Females >50 years d) Males >50 years
Q4	In what age group do you see SOD and BD more commonly? a) Females <50 years b) Males <50 years c) Females >50 years d) Males >50 years
Section 2: Etiology of BD	
Q5	Which risk factor is most commonly seen in your patients with BD? a) Long periods of fasting/total parental nutrition c) Drastic weight loss b) Recovering from major surgeries/stroke/heart attack/sepsis/extensive trauma d) Any other-please specify
Q6	In which setting have most of your patients developed BD? a) Outpatient department (ambulatory patients) b) Intensive care unit (critically ill) c) Hospital setting: Recovering from major surgery/illness d) Do not know/cannot say
Q7	How frequently have you seen obesity to be associated with BD? a) None of my patients b) Very few of my patients c) Many of my patients d) Almost all of my patients
Q8	What percentage of your patients are seen to suffer from SOD after cholecystectomy? a) <10% b) 11%-20% c) 21%-30% d) >31%
Q9	Which of the below risk factors have you found to be associated with SOD in your patients? a) Hypothyroidism b) Alcoholism c) Irritable bowel syndrome d) Preoperative cholelithiasis/gallstone lithotripsy
Section 3: Presentation of BD	
Q10	Which is the most common presenting symptom in your patients diagnosed with BD? a) Pain in right upper abdominal quadrant and epigastrium b) Bloating c) Dyspepsia/nausea d) Any other- please specify
Q11	What is the most common condition that BD mimics in your patients? a) Peptic ulcer disease b) B: Pancreatitis c) Colonic diverticular disease d) Cholelithiasis/Cholecystitis
Q12	In your experience have you found that BD patients with conditions that are different than those cause typical right upper quadrant abdominal pain? a) Yes, present as GERD b) B: Yes, present as IBS c) Yes, present as functional dyspepsia d) No, BD presents as a condition causing right upper quadrant abdominal pain only
Q13	Which condition is more commonly associated with BD in your patients? a) Gallbladder neuronal problems b) Diabetes mellitus c) Liver cirrhosis d) Chronic gallbladder inflammation
Q14	Have you found an associated of BD with other functional motility disorders in your patients? a) Yes, I have found an association with slow transition constipation b) Yes, I have found association with achalasia c) Yes, I have found association with gastroparesis d) No, I have not found any association with any other functional motility disorders.

Continued.

Questions				
Q15	The most common type of biliary SOD seen in your patients is:			
	A: Type I (biliary-type abdominal pain, with altered liver enzymes on blood testing and dilated biliary ducts)	b) Type II (biliary-type abdominal pain along with either altered liver enzymes on blood testing or dilated biliary ducts on imaging tests)		
	c) Type III (biliary-type pain in the absence of biliary duct alteration and normal liver function test)	d) I do not have sufficient data to comment		
Section 4: Investigations for BD				
Q16	What is your investigation of choice in suspected cases of BD?			
	a) Ultrasonography abdomen	b) Computed tomography scan abdomen	c) Cholescintigraphy (HIDA scan) with administration of cholecystokinin	d) Liver function tests
Q17	What is your preferred investigational method in suspected cases of SOD?			
	a) Magnetic resonance cholangiopancreatography	b) Sphincter of Oddi manometry	c) Ultrasonography	d) Hepatobiliary scintigraphy
Section 5: Perspectives on BD				
Q18	Do you think BD is an issue that burdens healthcare resources?			
	a) Yes, because of ambiguity in diagnosis	b) Yes, because of lack of consistency in management	c) Yes, because of significant presence in the community	
	d) No, I do not think it is an issue that burdens healthcare		e) Any other- please specify	
Section 6: Prognosis of BD				
Q19	What do you think is the chief reason for high failure rates of endoscopic and surgical treatments of SOD?			
	a) Difficulty in accurate diagnosis		b) Lack of specific objective criteria to select appropriate therapy	
	c) Possibility of SOD being part of generalized smooth muscle disorder of gastrointestinal tract		d) Other than these	
Q20	Which is the most common complication of BD seen in your experience?			
	a) Gallbladder perforation	b) Gallbladder gangrene	c) Sepsis	d) Multi-organ failure/acute respiratory distress syndrome
Q21	How successful would you say that laparoscopic cholecystectomy is, for improving symptoms of BD?			
	a) No resolution of symptoms in most of my patients	b) Partial resolution of symptoms in most of my patients	c) Complete resolution of symptoms in most of my patients	d) Cannot say
Q22	Of the patients who had experienced relief after cholecystectomy, how many of your patients have presented with classic biliary symptoms?			
	a) Almost all	b) Almost none. Most presented atypically	c) Some	d) Do not know/cannot say
Q23	In case of acute BD (acalculous cholecystitis) post gastric surgery, what is your preferred choice of management?			
	a) Cholecystectomy	b) Cholecystostomy	c) Percutaneous transhepatic gallbladder drainage	d) Antibiotic/medical management
Q24	What is your primary drug of choice in the medical treatment of functional gallbladder disorder?			
	a) CCBs	b) Antispasmodics	c) Gastrointestinal motility regulation drugs	d) Nitrates
	e) Multiple drugs (antispasmodic along with CCBs or GI motility regulating drugs)			
Q25	What is your preferred initial management of SOD?			
	a) CCBs	b) Nitrates	c) Botulinum toxin	d) Endoscopic sphincterotomy
Q26	What is your primary choice of drug in functional biliary sphincter of Oddi disorder?			
	a) Nifedipine/phosphodiesterase type-5 inhibitors	b) Antispasmodics	c) Nitrates	d) Motility regulators

Continued.

Questions				
Q27	What is your primary objective in prescribing pinaverium in biliary dysfunction?			
	a) Symptomatic action: pain relief	b) Therapeutic action: To reduce gallbladder/sphincter of Oddi contractions	c) Therapeutic action: To reduce bile duct pressure	d) Not have enough experience with pinaverium to comment
Q28	Which is the most common indication you prescribe pinaverium for?			
	a) Biliary SOD	b) Functional gallbladder dysmotility	c) Pancreatic SOD	d) Irritable bowel syndrome
Q29	What percentage of patients on pinaverium have complained of adverse effects (dry mouth, dry eyes, dizziness, acid reflux)?			
	a) <15%	b) 16%-25%	c) 26%-35%	d) >36%
Q30	Cardiovascular or systemic side effects of pinaverium bromide have been seen in __			
	a) None of my patients	b) Rare instances in my patients	c) Many of my patients	d) Do not know/cannot say
Q31	The most effective dosage of pinaverium in most of my patients is			
	a) 150 mg total daily dose	b) 200 mg total daily dose	c) 250 mg total daily dose	d) 300 mg total daily dose
Q32	What reduction in duration of pain have your patients reported with the use of pinaverium?			
	a) Pain reduced to duration of few hours	b) Pain reduced to duration of few minutes	c) No reduction in duration of pain	d) Not enough data to comment
Q33	How effective have you found pinaverium to be for abdominal pain in your patients?			
	a) Very effective	b) Somewhat effective	c) Not effective	d) Do not know/cannot say

BD, biliary dyskinesia; CCBs, calcium channel blockers; GI, gastrointestinal; HIDA, hepatobiliary iminodiacetic acid; SOD, sphincter of Oddi dysfunction

Table 2: Prevalence of BD and SOD in India.

Responses	N (%)
Prevalence of BD in patients with cholecystitis (%) (N=146)	
<10	111 (76.0)
11-20	26 (17.8)
21-30	7 (4.8)
>30	2 (1.4)
Prevalence of BD with associated SOD (%) (N=144)	
<25	122 (84.7)
26-50	10 (6.9)
51-75	6 (4.2)
>75	6 (4.2)
Gender and age association with SOD (years) (N=143)	
Females <50	92 (64.3)
Males <50	26 (18.2)
Females >50	35 (24.5)
Males >50	16 (11.2)
Gender and age association with BD (years) (N=114)	
Females <50	77 (67.5)
Males <50	20 (17.5)
Females >50	28 (24.6)
Males >50	9 (7.9)
Prevalence of type of SOD (N=145)	
Type I ^a	29 (20.0)
Type II ^b	26 (17.9)
Type III ^c	66 (45.5)
Lack of sufficient data to comment	24 (16.6)

BD, biliary dyskinesia; SOD, sphincter of Oddi dysfunction, ^abiliary-type abdominal pain, with altered liver enzymes on blood testing and dilated biliary ducts, ^bbiliary-type abdominal pain along with either altered liver enzymes on blood testing or dilated biliary ducts on imaging tests, ^cbiliary-type pain in the absence of biliary duct alteration and normal liver function test

Table 3: Risk factors for BD and SOD.

Parameters	N (%)
Most common risk factor for BD (N=115)	
Patients recovering from major surgeries/stroke/heart attack/sepsis/extensive trauma	61 (53.0)
Patients undergoing long periods of fasting/total parenteral nutrition	50 (43.5)
Drastic weight loss	28 (24.3)
Setting where BD is commonly encountered (N=135)	
Outpatient department (ambulatory patients)	73 (54.1)
Hospital setting: recovering from major surgery/illness	40 (29.6)
Intensive care unit (critically ill)	31 (22.9)
Obesity association with BD (N=146)	
None of my patients	19 (13.0)
Very few of my patients	92 (63.0)
Many of my patients	34 (23.3)
Almost all of my patients	1 (0.7)
Development of SOD after cholecystectomy (N=145) (%)	
<10	99 (68.3)
11-20	35 (24.1)
21-30	11 (7.6)
>31	0 (0.0)
Common risk factors for SOD (N=144)	
IBS	100 (69.4)
Preoperative cholelithiasis/gallstone lithotripsy	35 (24.3)
Alcoholism	11 (7.6)
Hypothyroidism	10 (6.9)

BD, biliary dyskinesia; IBS, irritable bowel syndrome; SOD, sphincter of Oddi dysfunction

Common conditions associated with BD were chronic gall bladder inflammation (56.2%), gall bladder neuronal problems (21.9%), and diabetes mellitus (21.9%). BD was not associated with other functional motility disorders according to 47.3% of physicians, whereas 28.1% and 23.3% stated that it was associated with gastroparesis and slow transition constipation, respectively (Table 4). According to the participating physicians, BD was an issue that burdened the healthcare resources because of ambiguity in diagnosis (70.5%), lack of consistency in its management (12.3%) and significant presence in the community (7.5%), whereas 16.4% did not think that BD burdened healthcare resources. BD may lead to complications if it remains undiagnosed and untreated. Common complications of BD as reported by participating physicians were sepsis (45.2%), gallbladder perforation (25.3%), gallbladder gangrene (18.5%), and multiorgan dysfunction/acute respiratory distress syndrome (5.5%).

Investigations and treatment modalities for the management of BD and SOD

Cholescintigraphy, hepatobiliary iminodiacetic acid (HIDA) scan with administration of cholecystokinin and hepatobiliary scintigraphy were identified as the most preferred investigations for diagnosis of BD and SOD by 55.5% and 33.6% of physicians, respectively (Table 5). Laparoscopic cholecystectomy was identified by 65.3% and 10.4% of physicians to result in partial and complete resolution of symptoms in most of their patients,

respectively, whereas 13.2% of physicians thought that this technique does not provide any resolution of symptoms and 11.1% of physicians were undecided. With regard to physicians' opinion on relief after cholecystectomy in patients with classical biliary symptoms, 42.5% and 35.6% stated that some and almost all patients experience relief, while 14.4% stated that none experience relief and 8.2% were undecided. For patients developing acute BD (acalculous cholecystitis) after gastric surgery, the most preferred management option was percutaneous transhepatic gallbladder drainage (43.2% participants), followed by cholecystectomy (22.6%) cholecystostomy (15.1%), and only medical management/antibiotic treatment (21.9%). The chief reason for the high failure rates with endoscopic and surgical treatment of SOD was difficulty in accurate diagnosis as indicated by 64.4% of participants, followed by possibility that SOD could be a part of generalized smooth muscle disorder of the gastrointestinal tract (24.0%) and lack of specific objective criteria to select appropriate therapy for SOD (13.0%). With regard to pharmacotherapy for functional gallbladder disorder, CCBs were preferred by 55.9% physicians and antispasmodics by 30.8% physicians (Table 5). For initial management of SOD, 63.4% of physicians preferred CCBs, while 29.0% preferred endoscopic sphincterotomy. For the treatment of functional biliary SOD, 52.8% preferred antispasmodics whereas 27.1% indicated nifedipine/phosphodiesterase 5 inhibitors (Table 5).

Table 4: Clinical presentation and comorbidities in BD and SOD (n=146).

Parameters	N (%)
Most common symptom of BD	
Pain in right upper abdominal quadrant and epigastrium	130 (89.0)
Bloating	18 (12.3)
Dyspepsia/nausea	25 (17.1)
Other (chest pain)	1 (0.7)
Conditions that mimic BD	
Cholelithiasis/cholecystitis	108 (74.0)
Peptic ulcer disease	27 (18.5)
Pancreatitis	15 (10.3)
Colonic diverticular disease	9 (6.2)
Differential diagnosis for BD presenting with typical right upper quadrant abdominal pain	
GERD	6 (4.1)
IBS	38 (26.0)
FD	74 (50.7)
None	36 (24.7)
Conditions associated with BD	
Chronic gallbladder inflammation	82 (56.2)
Gallbladder neuronal problems	32 (21.9)
Diabetes mellitus	32 (21.9)
Liver cirrhosis	13 (8.9)
Other functional motility disorders associated with BD	
Gastroparesis	41 (28.1)
Slow transition constipation	34 (23.3)
Achalasia	3 (2.1)
None	69 (47.3)

BD, biliary dyskinesia; FD, functional dyspepsia; GERD, gastroesophageal reflux disease; IBS, irritable bowel syndrome; SOD, sphincter of Oddi dysfunction

Physicians' experience with pinaverium in the management of BD

Pinaverium is an antispasmodic used in the management of functional gastrointestinal disorders. According to the participating physicians in this survey, the primary objective to prescribe pinaverium for BD was pain relief as indicated by 42.5% of the participants, reducing gall bladder or sphincter of Oddi contraction according to 18.5% of participants, and reducing bile duct pressure according to 6.85% of participants, while 36.3% participants stated that they did not have enough experience with pinaverium. The most common indication for which pinaverium was prescribed by the participating physicians was IBS (84.0%; Table 6). Majority (86.9%) of the physicians reported that adverse effects with pinaverium such as dry mouth, dry eyes, dizziness, and acid reflux were found to be present in <15% of patients in their clinical practice, while 68.1% of physicians indicated absence of cardiovascular or systemic side effects with pinaverium in their patients. The most effective dose of pinaverium was 150 mg per day according to 93.1% of the physicians, pain reduction after pinaverium use was observed within a few hours by nearly 70% of the physicians, and pinaverium was identified to be very effective for abdominal pain by 73.1% of physicians (Table 6).

DISCUSSION

Functional gastrointestinal disorders are characterized by morphological and physiological abnormalities. In this survey, we assessed the practices of Indian gastroenterologists in diagnosis and treatment of BD and SOD given the relative lack of large-scale epidemiological studies. BD might be present in patients with present with biliary pain. Majority of the physicians in our survey indicated that <10% of patients with cholecystitis get diagnosed with BD. This is due to the symptom overlap of two conditions. Post-cholecystectomy, on pathological examination, the gall bladder of patients with BD can demonstrate chronic cholecystitis and cholesterosis.⁹ BD may be secondary to SOD. Majority of the of surveyed physicians opined that <25% of their patients with BD have SOD. In a study from Corazziari et al out of 34 patients with BD, 28% and 44% had the sphincter of Oddi hypertension and hypotonia, respectively.¹⁰ Although SOD can occur at any age and in either sex, it is known to affect females more than males, and females between ages 20 and 40 years are commonly affected.⁵ It was clear from our survey, majority of the participants indicated females <50 years were frequently identified with SOD. Similarly, BD is also more common in females of this age group. This finding suggests that female patients aged <50 years presenting with biliary symptoms in the absence of gall bladder disease should be assessed further for BD or SOD.

Table 5: Preferred investigations and treatment modalities for BD and SOD.

Parameters	N (%)
Investigation of choice for suspected BD (N=146)	
Abdomen ultrasonography	19 (13.0)
Abdomen computed tomography	2 (1.4)
Cholescintigraphy (HIDA scan) with administration of cholecystokinin	81 (55.5)
Liver function tests	14 (9.6)
Combined (one or more investigations)	30 (20.5)
Investigation of choice for suspected SOD (N=146)	
Magnetic resonance cholangiopancreatography	35 (24.0)
Sphincter of Oddi manometry	25 (17.1)
Ultrasonography	20 (13.7)
Hepatobiliary scintigraphy	49 (33.6)
Combined (one or more investigations)	17 (11.6)
Primary drug of choice for functional gallbladder disorder (N=146)	
CCBs	80 (55.9)
Antispasmodics	44 (30.8)
Gastrointestinal motility regulation drugs	4 (2.8)
Nitrates	5 (3.5)
Multiple drugs (antispasmodic along with CCBs or GI motility regulating drugs)	10 (7.0)
Initial management of SOD (N=145)	
CCBs	92 (63.4)
Endoscopic sphincterotomy	42 (29.0)
Nitrates	11 (7.6)
Primary drug of choice for functional biliary sphincter of Oddi disorder (N=144)	
Nifedipine/phosphodiesterase type-5 inhibitors	39 (27.1)
Antispasmodics	76 (52.8)
Nitrates	11 (7.6)
Motility regulators	8 (5.6)
Combined (one or more)	10 (6.9)

BD, biliary dyskinesia; CCBs, calcium channel blockers; GI, gastrointestinal; HIDA, hepatobiliary iminodiacetic acid
SOD, sphincter of Oddi dysfunction

Risk factors for the development of BD can be difficult to identify. In our survey, physicians identified that patients recovering from major surgeries/stroke/heart attack/sepsis/extensive trauma and patients undergoing long periods of fasting or those on total parenteral nutrition are at risk for BD. Though obesity has been reported to be associated with gallstone,¹¹ majority of participants in this survey reported that obesity was seen in very few patients with BD in their clinical practice. The prevalence of various comorbidities does not differ between patients with and without BD.¹² In the present survey, IBS was identified as risk factor for SOD followed by cholelithiasis. Post-cholecystectomy, SOD was reported to be seen in nearly 11%-20% of the patients.¹³ Post-cholecystectomy SOD might be a component of a more generalized intestinal motor disorder.¹⁴ This is possibly also the reason for the association of SOD with IBS.¹⁵ The clinical presentation is similar to other gall bladder disorders that cause characteristic biliary pain. Diagnostic criteria for BD necessitate presence of characteristic biliary pain in absence of gallstones supported by low ejection fraction on gallbladder scintigraphy with normal

liver function tests and pancreatic enzyme levels.¹⁶ This is the main reason that majority of participants indicated BD mimics cholelithiasis/cholecystitis. In differential diagnosis of BD with typical right upper quadrant abdominal pain, FD, GERD, and IBS can be present. Most physicians in this survey identified that FD may be seen in patients with BD. Chronic gallbladder inflammation has been identified as important factor associated with BD. In causation of BD, impaired gallbladder emptying, chronic inflammation, visceral hypersensitivity, and panenteric motility disorders are proposed. In BD, chronic inflammatory changes ranging from 44% to 100% have been reported.¹⁷ Despite the possibilities of association with other motility disorders, 47.3% participants disagreed that BD is associated with other such disorders. A few participants reported association of BD with slow transition constipation and gastroparesis. Among the different types of SOD, 47.3% participants reported type III SOD as the most common type observed in their clinical setting. Type III is classified as biliary type pain in the absence of any objective finding of liver test abnormalities and bile duct dilatation. Type III SOD likely represents a right upper quadrant functional abdominal pain syndrome.¹⁸

Table 6: Current place of pinaverium in abdominal ailments.

Parameters	N (%)
Most common indication for prescribing pinaverium (N=144)	
IBS	121 (84.0)
Biliary SOD	17 (11.8)
Functional gallbladder dysmotility	13 (9.0)
Pancreatic SOD	2 (1.4)
Proportion of patients with adverse effects of pinaverium* (N=145)	
<15%	126 (86.9)
16-25%	11 (7.6)
26-35%	7 (4.8)
Cardiovascular or systemic side effects of pinaverium (N=144)	
None	98 (68.1)
Rare	32 (22.2)
Many patients	5 (3.5)
Cannot say	11 (7.6)
Most effective dosage of pinaverium (N=145)	
150 mg total daily dose	135 (93.1)
200 mg total daily dose	6 (4.1)
250 mg total daily dose	2 (1.4)
300 mg total daily dose	2 (1.4)
Duration of pain reduction with pinaverium (N=145)	
Few hours	102 (70.3)
Few minutes	34 (23.4)
No reduction in duration of pain	2 (1.4)
Not enough data to comment	8 (5.5)
Effectiveness of pinaverium for abdominal pain (N=145)	
Very effective	106 (73.1)
Somewhat effective	36 (24.8)
Not effective	2 (1.4)
Cannot say	2 (1.4)

*dry mouth, dry eyes, dizziness, acid reflux, IBS, irritable bowel syndrome; SOD, sphincter of Oddi dysfunction

Investigations for these disorders are important for diagnosis. Abdominal ultrasound is normal in these cases and thus cholecystigraphy is the test of choice for suspected BD.¹⁷ Cholecystigraphy (HIDA scan) with administration of cholecystokinin was identified to be the investigation of choice by majority of the physicians in our survey. This investigation is helpful in the function assessment of gallbladder with estimation of gallbladder ejection fraction. A low ejection fraction indicates impaired function of the gallbladder.¹⁷ For SOD diagnosis, physicians suggested hepatobiliary scintigraphy, magnetic resonance cholangiopancreatography, sphincter manometry study, and ultrasonography. All these investigations are useful for SOD diagnosis. Manometry is the gold standard for diagnosis of SOD.¹⁹ However, in resource-limited settings, ultrasound may provide clues to diagnosis. Dilatation of common bile duct by >6 mm could indicate possibility of SOD. Its utility can further be improved with use of provocative tests.⁵ Hepatic scintigraphy has been shown to have good correlation with manometry.²⁰ Despite the availability of non-invasive and invasive diagnostic methods, there remains ambiguity in diagnosis that has been agreed by majority of the participants. This puts extra burden on the healthcare resources. Laparoscopic cholecystectomy is widely used

as treatment of BD. Nearly 2/3rd of the physicians stated that they observe partial resolution of symptoms in most patients, regardless of presentation with classic biliary symptoms. A recent study by Whitaker et al reported partial or complete resolution of symptoms in 92.3% patients after laparoscopic cholecystectomy.⁶ Post-surgery acute BD is effectively managed with percutaneous transhepatic gallbladder drainage (PTGBD). This was agreed upon by the 43.2% of the participants. Studies indicate effective utility PTGBD in acute BD following major surgeries.^{21,22} Surgical therapy failure in SOD is mainly because of difficulty in diagnosis, which was indicated by 64.4% of the participants. CCBs were identified as the primary therapy of choice for BD and SOD. Sublingual nifedipine has been shown to reduce the pain in 75% of patients with SOD.²³ Nitrates also effectively reduce sphincter pressure and provide symptomatic relief. Endoscopic sphincterotomy remains a choice in SOD. Compared to surgery, endoscopy is preferred. Patients who have elevated pressures at baseline have highest benefit after sphincterotomy.⁵ For functional biliary sphincter of Oddi disorder, antispasmodics were the most preferred agents by 56.8% of the physicians. A study from the United Kingdom reported that among 59 patients with biliary SOD (14%, type I; 51%, type II; 35%, type

III), 51% had symptom resolution with medications only, 12% with sphincterotomy, and 10% with use of both medical and surgical approaches.²⁴

Pinaverium bromide is a selective CCB that exerts antispasmodic effect in the gastrointestinal tract. In addition, it inhibits the effect of contractile hormones in the gastrointestinal tract.²⁵ In assessing the role of pinaverium, it was found to be primarily prescribed for pain relief in BD as indicated by 42.5% of the participants. Interestingly, 36.3% did not have enough experience with pinaverium, indicating that it may be reserved or preferred in specific situations. Pinaverium has shown some benefit in symptom relief among patients with BD.²⁶ In this context, majority of the physicians in our survey indicated that they use pinaverium in IBS. A recent meta-analysis of eight randomized placebo-controlled trials demonstrated significant effect in overall IBS symptom relief with numbers needed to treat identified to be four.²⁷ It is clear that pinaverium can be useful in functional gastrointestinal disorders that are possibly associated with gastrointestinal dysmotility. Pinaverium related adverse events (AEs) such as dry mouth, dry eyes, and dizziness were reported to be present in <15% of patients by majority of the participants. In another study, the incidence of AEs such as nausea, dizziness, increased blood pressure, and abdominal discomfort was reported to be <5%.²⁸ Our survey identified the 150 mg/day dose to be effective in most patients. Being a spasmolytic, it reduces pain, at least for few minutes or hours as suggested by the survey participants. It has been reported to be very effective for pain reduction by majority of the surveyed gastroenterologists. Thus, pinaverium can be considered for unspecified abdominal pain pending the accurate diagnosis of the same.

Our survey has certain strengths and limitations. The major strength of this survey is in the fact that it provides pan-India evidence on the practices of gastroenterologists on effective assessment, diagnosis and treatment of BD and SOD. Given the limited evidence from India, our survey highlights important facts about the management of BD and SOD in the Indian context. Our study is limited by opinions and practices of physicians and not actual inclusion of patients. Cross-sectional nature of the survey does not address the changes in practices over time. Nonetheless, the survey generates additional evidence pertaining to BD and SOD in Indian region.

CONCLUSION

Functional gall bladder disorder and SOD are disorders of the biliary tract characterized by dysmotility and biliary pain. In absence of relative lack of studies from India, the findings of this survey hold potential for further research in these rare disorders. Principally, we identify that BD and SOD are common in females aged <50 years who present with classical biliary pain symptoms. Given the rarity of these disorders, they pose a significant diagnostic challenge especially in resource-limited settings. Despite

some contradictory evidence, cholecystectomy can provide partial or complete symptom relief in BD. SOD management mainly relies on endoscopy or surgery. Combined with medical and surgical treatment, better outcomes may be achieved in these functional biliary disorders.

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