



Management of bile acid diarrhea in Italy: a survey

Giovanni Marasco^{1,2} · Giovanni Barbara^{1,2} · Massimo Bellini³ · Piero Portincasa⁴ · Vincenzo Stanghellini² · Bruno Annibale⁵ · Antonio Benedetti⁶ · Giovanni Cammarota⁷ · Walter Fries⁸ · Paolo Usai Satta⁹ · Enrico Stefano Corazziari¹⁰

Received: 17 April 2025 / Accepted: 8 July 2025 / Published online: 12 September 2025
© The Author(s) 2025

Abstract

Bile acid diarrhea (BAD) is a common, under-investigated cause of chronic diarrhea. We aimed to assess the current management of BAD among a group of Italian physicians. A survey was developed by a task force of experts and distributed via the Internet to Italian physicians members of the main Italian gastroenterological associations. Ninety-four physicians accepted to participate, of whom 44% were females. The majority of participants were gastroenterologists (63%) and the mean age was 50.5 years. No differences in the rate of BAD diagnosis among patients with chronic diarrhea were found according to medical specialization. Gastroenterologists reported a higher prevalence of BAD compared with other physicians/general practitioners (1% vs 0.3%). BAD suspicion is mostly raised in the presence of watery stools and > 3 bowel movements/day and the exclusion of organic/drug-related diseases. BAD diagnosis was assessed with ⁷⁵SeHCAT (67.8% of gastroenterologists and 51.4% of other physicians), followed by a trial of cholestyramine (30.5% of gastroenterologists and 31.4% of other physicians). Therapies most prescribed for BAD were cholestyramine, a low-fat diet, and stool thickeners. BAD is a common condition generally suspected in the presence of chronic watery diarrhea. ⁷⁵SeHCAT availability influences the awareness of this disease. Therapies currently are often not able to guarantee adequate symptom relief.

Keywords Bile acid diarrhea · Cholestyramine · Colesevelam · Diarrhea · Irritable bowel syndrome · Survey

Introduction

Bile acid malabsorption (BAD) is a common under-investigated cause of chronic diarrhea (25–33%) with a prevalence of about 1% in the general population [1–3]. About 25–33% of unexplained chronic diarrhea is due to BAD and it is also present in about one-third of patients with irritable bowel syndrome diarrhea-predominant (IBS-D) [4–6]. BAD results

from dysregulation of the enterohepatic recirculation of bile acids (BAs) and its consequent alteration of bile acid production driven by several mechanisms [7]. It finally hesitates in an excessive level of BAs in the lower gastrointestinal tract, which in turn can stimulate water and sodium excessive transport, mucosal damage, mucus secretion, increased lower gastrointestinal motility, and stimulation of defecation

✉ Giovanni Marasco
giovanni.marasco4@unibo.it

¹ IRCCS Azienda Ospedaliero Universitaria Di Bologna, Bologna, Italy
² Department of Medical and Surgical Sciences, University of Bologna, Bologna, Italy
³ Gastrointestinal Unit, Department of Translational Research and New Technologies in Medicine and Surgery, University of Pisa, Pisa, Italy
⁴ Clinica Medica “A. Murri”, Department of Precision and Regenerative Medicine and Ionian Area (DiMePre-J), University of Bari Aldo Moro, Bari, Italy

⁵ Department of Medical-Surgical Sciences and Translational Medicine, Sant’Andrea Hospital, Sapienza University of Rome, Rome, Italy

⁶ Clinic of Gastroenterology and Hepatology, Università Politecnica Delle Marche, Ospedali Riuniti-University Hospital, Ancona, Italy

⁷ Gastroenterology Unit, Fondazione Policlinico A Gemelli IRCCS, Catholic University of Medicine, Rome, Italy

⁸ Clinical Unit of Gastroenterology, Department of Clinical and Experimental Medicine, University of Messina, Messina, Italy

⁹ Gastroenterology Unit, ARNAS G. Brotzu, Cagliari, Italy

¹⁰ Department of Gastroenterology, IRCCS Humanitas Research Hospital, Rozzano, Milano, Italy

[8–10], finally leading to BA-associated diarrhea (BAD). Therefore, patients with BAD complain of increased frequency of watery chronic diarrhea, fecal urgency, abdominal pain, bloating, and fecal incontinence [11]. Affected individuals may also report systemic symptoms including fatigue, dizziness and feeling of fainting [12]. Currently, the gold standard diagnostic method for identifying BAD and assessing its degree of severity is the 75-Selenium-HomotauroCholic Acid Test (75SeHCAT), consisting of a radio-labelled synthetic conjugated bile acid (23-seleno-25-homotauro-cholic acid) that is orally administered, secreted in bile and then reabsorbed in the terminal ileum [13]. According to the retention of this radio-labeled marker it is possible to ascertain the presence and severity of BAD, which is directly correlated to the response to bile acid sequestrants [14]. Other diagnostic markers have been recently proposed, such as 7 α C4 or FGF19 [15–18]. However, also due to the insufficient availability of diagnostic tests and the lack of awareness among physicians on this condition, BAD is often overlooked and misdiagnosed, leading to delayed diagnosis up to 5 years after symptom onset [14]. The diagnostic delay impacts the quality of life of affected individuals and increases the healthcare burden with unnecessary diagnostic tests [19]. Current treatment for these patients includes dietary modification and the use of bile acid sequestrants (BASTs, e.g. cholestyramine, colestevlam, colestipol) [7]. However, BASTs are often ineffective when used in uninvestigated patients or poorly tolerated due to side effects such as constipation, abdominal pain, bloating, fullness, nausea, and flatulence [20], and the poor palatability of cholestyramine and colestipol, which result in low compliance.

We aimed to assess the current knowledge and management of BAD among a group of Italian physicians in order to increase awareness of this condition and target possible knowledge gaps in the near future within this field.

Methods

A survey investigating BAD knowledge and management in Italy was developed by a task force of experts (GB, MB, VS, ESC).

The survey was developed in Italian and consisted of 22 questions, including different areas of interest: (a) demographics and work position, (b) knowledge of BAD epidemiology and management, and (c) personal clinical experience of BAD. Survey questions and responses are available in Tables 1 and 2. The electronic survey was distributed via Internet to Italian physicians with an interest in gastroenterology and to members of the main Italian gastroenterological associations between May and September 2022. A secured online survey was provided by a professional company (Qualtrics, LLC, Provo, UT). The survey was anonymous

and had built-in quality-assurance measures to exclude poor-quality responders. The software ensured that there were no missing answers to compulsory questions and had automated skip patterns, resulting in complete and accurate symptom pattern information.

Statistical analysis

Data are presented as counts and percentages for the categorical variables and mean and standard deviation (SD) for the continuous variables. The categorical variables were compared using the Chi-squared or Fisher's exact tests as appropriate. For multiple categorical variables, the Chi-squared test of independence was used. The continuous variables were compared using the t-test or the Kruskal–Wallis test as appropriate. The differences in responses between gastroenterologists and other physicians, as well as between physicians with and without regional availability of 75SeHCAT were calculated. The probability values were two-sided; a probability value of less than 0.05 was considered statistically significant. Statistical analysis was performed with STATA 17.0 (SE, Standard Edition, College Station, TX: StataCorp LP).

Results

Participants' demographics and clinical experience

Ninety-four participated in the survey, of whom 47 were females (44%). The majority of participants were gastroenterologists (63%), while the remaining 37% included internal medicine physicians (12.8%), general surgeons (3%), general practitioners (9.6%) and other healthcare professionals (11.6%).

Tables 1 and 2 report survey question responses according to medical specialization and 75SeHCAT availability, respectively. The mean age of participants was 50.5 years (SD 16.4), with a significantly older age in the group of gastroenterologists (54.5 years) compared to other physicians (43.4 years) ($p < 0.001$). No differences were found according to 75SeHCAT availability. About half of the participants (48%) were from Northern Italy, 26% from Central and 26% from Southern Italy. No differences in geographical areas of origin were found according to medical specialization or 75SeHCAT availability.

Gastroenterologists reported to visit a significantly higher number of patients with chronic diarrhea when compared to other physicians (149.8 vs 77.8, $p = 0.002$). However, no differences in the rate of BAD diagnosis within patients with chronic diarrhea were found among the two groups. Different estimations of BAD prevalence in the general population were reported by the two groups since gastroenterologists

Table 1 Response to survey questions according to medical specialization

	Gastroenterologist <i>N</i> (%) or mean (SD) <i>n</i> = 59	Other physicians <i>N</i> (%) or mean (SD) <i>n</i> = 35	<i>P</i>
Sex (Female)	22 (37.2)	19 (54.3)	0.108
Age	54.5 (15.5)	43.4 (15.7)	<0.001
Geographical area			
Northern Italy	29 (49.2)	16 (45.7)	0.747
Central Italy	16 (27.1)	8 (22.9)	0.647
Southern/Islands Italy	14 (23.7)	11 (31.4)	0.414
Rate of patients with BAD in the general population			
0.3%	16 (27.1)	17 (48.6)	0.035
0.05%	7 (11.9)	3 (8.6)	0.617
1%	24 (40.7)	7 (20)	0.039
10%	4 (6.8)	0 (0)	0.293
I don't know	8 (13.6)	8 (22.9)	0.246
Number of patients/year with chronic diarrhea	149.8 (188.3)	77.8 (106.3)	0.002
Rate of patients among those with chronic diarrhea with BAD	12.6 (21.3)	7.2 (9.1)	0.205
Clinical suspicion of BAD			
Watery stools	0	1 (2.9)	0.372
Watery stools and > 3 CSBM/day	1 (1.7)	1 (2.9)	0.706
Watery stools and exclusion of organic/drug-related diseases	4 (6.8)	6 (17.1)	0.115
Watery stools and > 3 CSBM/day and exclusion of organic/drug-related diseases	36 (61)	23 (65.7)	0.649
Watery stools and > 3 CSBM/day not responsive to previous therapies	18 (30.5)	4(11.4)	0.035
Diagnostic evaluation for BAD			
Colonoscopy and biopsies	0	4 (11.4)	0.017
Cholestyramine therapy response	18 (30.5)	11 (31.4)	0.926
Budesonide therapy response	0	0	1
75SeHCAT	40 (67.8)	18 (51.4)	0.115
Other	1 (1.7)	2 (5.7)	0.283
Dose of cholestyramine used for ex-adiuvantibus diagnosis			
2 g/die	3 (16.7)	2 (18.2)	0.917
4 g/die	5 (27.8)	7 (63.6)	0.057
6 g/die	1 (5.6)	1 (9.1)	0.715
8 g/die	7 (38.9)	1 (9.1)	0.082
Other	2 (11.1)	0	0.512
Duration of cholestyramine therapy for ex-adiuvantibus diagnosis (days)			
3	0	0	1
7	2 (11.1)	5 (45.5)	0.036
10	3 (16.7)	3 (27.3)	0.494
14	4 (22.2)	2 (18.2)	0.794
28	9 (50)	1 (9.1)	0.041
Belief that 75SeHCAT diagnosis is better than empiric therapy			0.293
Yes	26 (44.1)	17 (50)	
No	17 (28.8)	5 (14.7)	
I don't know	16 (27.1)	12 (35.3)	
Perceived diagnostic accuracy of 75SeHCAT for BAD diagnosis			
20–30%	1 (1.7)	2 (5.9)	0.284
60–70%	25 (42.4)	15 (44.1)	0.963
90–100%	26 (44.1)	9 (26.5)	0.075
I don't know	7 (11.9)	8 (23.5)	0.160
75SeHCAT prescription in clinical activity (if ever requested)	22 (37.3)	9 (26.5)	0.287

Table 1 (continued)

	Gastroenterologist <i>N</i> (%) or mean (SD) <i>n</i> = 59	Other physicians <i>N</i> (%) or mean (SD) <i>n</i> = 35	<i>P</i>
Regional availability of ⁷⁵ SeHCAT			0.004
Yes	26 (46.4)	12 (37.5)	
No	14 (25)	1 (3.1)	
I don't know	16 (28.6)	19 (59.4)	
Number of ⁷⁵ SeHCAT prescribed in the last year	3.2 (20)	2.8 (9.1)	0.213
Belief that ⁷⁵ SeHCAT test is enough for BAD diagnosis			0.059
Yes	41 (73.2)	16 (50)	
No	7 (12.5)	5 (15.6)	
I don't know	8 (14.3)	11 (34.4)	
Belief that 7αC4 or FGF19 are enough accurate for BAD diagnosis			0.644
Yes	11 (19.6)	6 (18.7)	
No	17 (30.4)	7 (21.9)	
I don't know	28 (50)	19 (59.4)	
Satisfied by therapies available for BAD	19 (33.9)	10 (31.3)	0.797
Rate of patients with BAD with satisfying symptom control and quality of life	54.7 (26.2)	42.4 (30)	0.070
Satisfied about own knowledge of BAD	14 (25)	6 (18.8)	0.501
Belief in the usefulness of updates on BAD	55 (98.2)	32 (100)	0.447

mainly reported a prevalence of about 1% (40.7% of gastroenterologists), while other physicians mainly reported an estimated prevalence of 0.3% (48.6% within this group). No differences in the number of visits for chronic diarrhea and BAD estimation were found according to ⁷⁵SeHCAT availability.

BAD diagnosis

The presence of watery stools, > 3 complete spontaneous bowel movement (CSBM)/day and the exclusion of organic/drug-related diseases were identified as a criterion for BAD diagnosis by most respondents to the survey, without differences among groups except for about one-third of gastroenterologists which additionally reported to suspect BAD in case of failure of previous therapies for chronic diarrhea. BAD diagnosis was generally reported to be assessed by ⁷⁵SeHCAT (67.8% of gastroenterologists and 51.4% of other physicians; *p* = 0.115), followed by the assessment of the clinical response to a trial of cholestyramine (30.5% of gastroenterologists and 31.4% of other physicians; *p* = 0.926). As expected, ⁷⁵SeHCAT was the most prescribed test, based on regional availability (84.2% when ⁷⁵SeHCAT available vs. 46.4% when unavailable, *p* < 0.001). The cholestyramine trial test was prescribed by 42.9% of physicians without ⁷⁵SeHCAT regional availability.

Among the 29 participants reporting adopting ex adjuvantibus diagnostic criteria based on cholestyramine therapy, no differences were found between gastroenterologists and other physicians, nor according to ⁷⁵SeHCAT availability

in terms of doses employed. Overall, 17% of participants reported using 2 g/die, 41.4% of participants 4 g/die, 6.9% of participants 6 g/die, 27.6% of participants 8 g/die and 6.9% other amounts. When the duration of the cholestyramine trial for ex adjuvantibus diagnosis was considered, 24.4% of participants reported a trial of 7 days, 20.7% of 10 days, 20.7% of 14 days and 34.5% of 28 days. About half of the other physicians adopted a 7-days trial, while half of the gastroenterologists 28 days. No differences were found according to ⁷⁵SeHCAT availability.

Only about half of the participants believed that a BAD diagnosis using the ⁷⁵SeHCAT test was more accurate than using an ex adjuvantibus diagnosis with a cholestyramine trial, without differences between groups.

Overall, one-third of participants reported having prescribed ⁷⁵SeHCAT in their routine clinical practice.

No differences in the number of participants prescribing ⁷⁵SeHCAT and in the number of ⁷⁵SeHCAT prescribed were found according to medical specialization, while huge differences were found according to ⁷⁵SeHCAT availability (65.8% of prescribers when locally available vs 10.9% when unavailable, *p* < 0.001 and a mean of 6.5 ⁷⁵SeHCAT/per year prescribed when available vs 0.5 when unavailable, *p* < 0.001).

When BAD was confirmed by ⁷⁵SeHCAT the most frequent diagnoses were idiopathic BAD in the majority of cases, followed by post-surgical BAD (both post-cholecystectomy and post-ileal resection), small intestinal bacterial overgrowth, and others (Fig. 1A). When BAD was not confirmed by ⁷⁵SeHCAT, the final diagnoses causing chronic

Table 2 Response to survey questions according to 75SeHCAT regional availability

	No 75SeHCAT availability <i>N</i> (%) or mean (SD) <i>n</i> = 56	75SeHCAT availability <i>N</i> (%) or mean (SD) <i>n</i> = 38	<i>P</i>
Sex (Female)	25 (44.6)	16 (42.1)	0.808
Age	50.6 (15.7)	50.3 (17.6)	0.896
Geographical area			
Northern Italy	24 (42.9)	21 (55.3)	0.237
Central Italy	14 (25)	10 (26.3)	0.886
Southern/Islands Italy	18 (32.1)	7 (18.4)	0.140
Rate of patients with BAD in the general population			
0.3%	17 (30.4)	16 (42.1)	0.097
0.05%	8 (14.3)	2 (5.3)	0.197
1%	16 (28.6)	15 (39.5)	0.270
10%	1 (1.8)	3 (7.9)	0.150
I don't know	14 (25)	2 (5.3)	0.124
Number of patients/year with chronic diarrhea	102.8 (110.5)	154.9 (224.2)	0.272
Rate of patients among those with chronic diarrhea with BAD	9.3 (13.6)	12.6 (23.1)	0.666
Clinical suspicion of BAD			
Watery stools	0	1 (2.6)	0.409
Watery stools and > 3 CSBM/day	2 (3.6)	0	0.513
Watery stools and exclusion of organic/drug-related diseases	5 (8.9)	5 (13.2)	0.514
Watery stools and > 3 CSBM/day and exclusion of organic/drug-related diseases	35 (62.5)	24 (63.2)	0.948
Watery stools and > 3 CSBM/day not responsive to previous therapies	14 (25)	8 (21.1)	0.657
Key diagnostic evaluation for BAD			
Colonoscopy and biopsies	3 (5.4)	1 (2.6)	0.521
Cholestyramine therapy response	24 (42.9)	5 (13.2)	0.002
Budesonide therapy response	0	0	1
75SeHCAT	26 (46.4)	32 (84.2)	<0.001
Other	3 (5.4)	0	0.270
Dose of cholestyramine used for ex-adiuvantibus diagnosis (in cholestyramine users)			
2 g/die	4 (16.7)	1 (20)	0.857
4 g/die	11 (45.8)	1 (20)	0.286
6 g/die	2 (8.3)	0	1
8 g/die	6 (25)	2 (40)	0.495
Other	1 (4.2)	1 (20)	0.204
Duration of cholestyramine therapy for ex-adiuvantibus diagnosis (in cholestyramine users), days			
3	0	0	1
7	6 (25)	1 (20)	0.812
10	6 (25)	0	0.553
14	5 (20.8)	1 (20)	0.967
28	7 (29.2)	3 (60)	0.187
Belief that 75SeHCAT diagnosis is better than empiric therapy			0.977
Yes	25 (45.5)	18 (47.4)	
No	13 (23.6)	9 (23.7)	
I don't know	17 (30.9)	11 (28.9)	
Perceived diagnostic accuracy of 75SeHCAT for BAD diagnosis			
20–30%	2 (3.6)	1 (2.6)	0.799
60–70%	20 (36.4)	20 (52.6)	0.104
90–100%	20 (36.4)	15 (39.5)	0.711

Table 2 (continued)

	No 75SeHCAT availability <i>N</i> (%) or mean (SD) <i>n</i> = 56	75SeHCAT availability <i>N</i> (%) or mean (SD) <i>n</i> = 38	<i>P</i>
I don't know	13 (23.6)	2 (5.3)	0.020
75SeHCAT prescription in clinical activity (if ever requested)	6 (10.9)	25 (65.8)	<0.001
Number of 75SeHCAT prescribed in the last year	0.5 (2.2)	6.5 (25.2)	<0.001
Belief that 75SeHCAT test is enough for BAD diagnosis			0.004
Yes	31 (62)	26 (68.4)	
No	3 (6)	9 (23.7)	
I don't know	16 (32)	3 (7.9)	
Belief that 7αC4 or FGF19 are enough accurate for BAD diagnosis			0.081
Yes	11 (22)	6 (15.8)	
No	9 (18)	15 (39.5)	
I don't know	30 (60)	17 (44.7)	
Satisfied by therapies available for BAD	16 (32)	13 (34.2)	0.827
Rate of patients with BAD with satisfying symptom control and quality of life	46.2 (29.3)	56.5 (25.4)	0.144
Satisfied about own knowledge of BAD	4 (8)	16 (42.1)	<0.001
Belief in the usefulness of updates on BAD	49 (98)	38 (100)	0.381

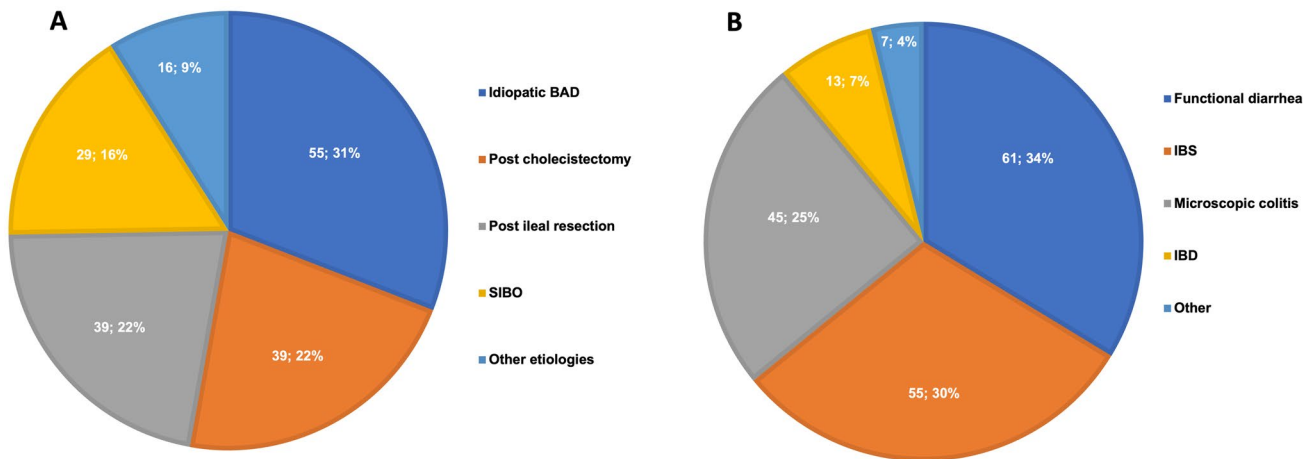


Fig. 1 Diagnosis after 75SeHCAT testing in patients with chronic unexplained diarrhea reported by respondents in their own experience: **A** BAD subtypes (%) and **B** other diagnosis after BAD exclu-

sion (%) (multiple answers were allowed). *Abbreviations: BAD, bile acid malabsorption; SIBO, small intestinal bacterial overgrowth; IBS, irritable bowel syndrome; IBD, inflammatory bowel diseases*

diarrhea were functional diarrhea, irritable bowel syndrome, microscopic colitis and inflammatory bowel diseases in decreasing order of reported occurrence (Fig. 1B).

Only about 20% of respondents supported the accuracy of 7αC4 or FGF19 for BAD diagnosis, without differences between groups.

BAD management

Overall, 33% of participants reported being satisfied with the currently available therapies for BAD, without differences between groups. The most commonly prescribed therapies were cholestyramine, a low-fat diet, stool thickeners (i.e. diosmectite), and loperamide (Fig. 2). About half of the respondents from both groups reported to have achieved symptom control in less than 50% of patients. The overall satisfaction about the personal knowledge

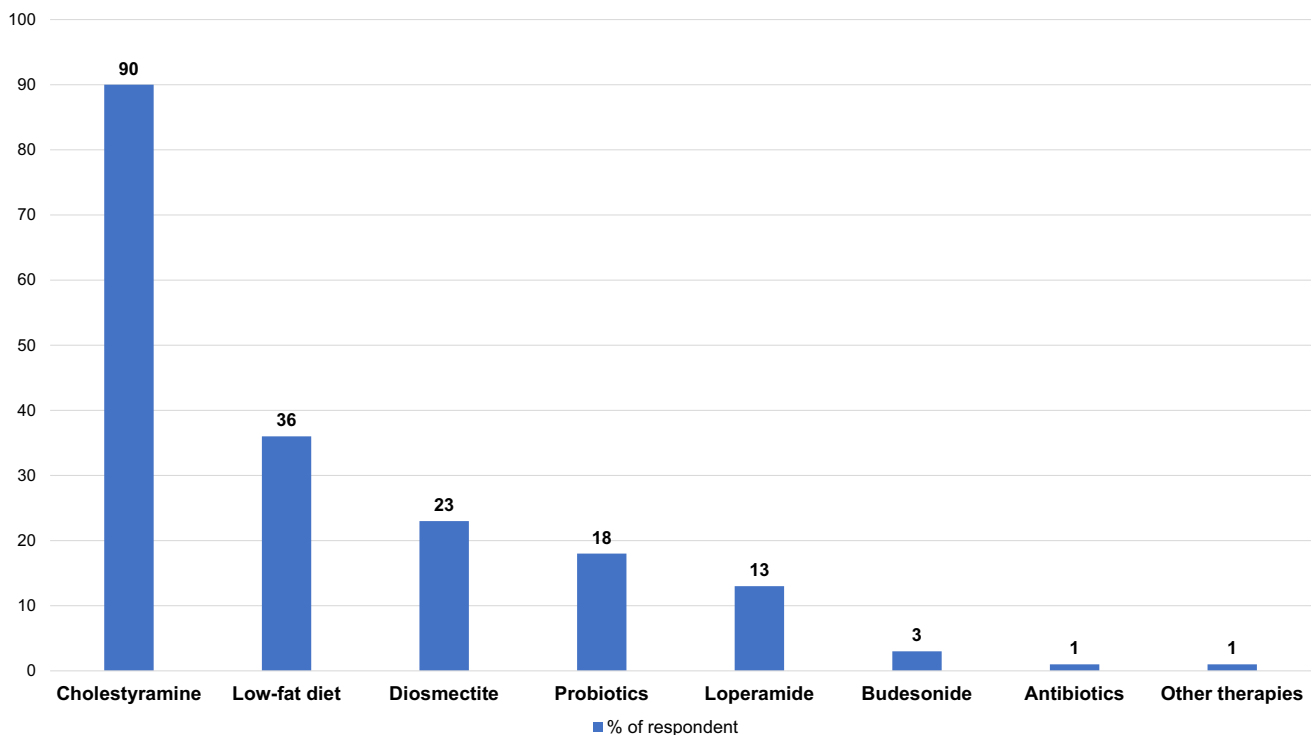


Fig. 2 Therapies most commonly prescribed for BAD reported by participants in the survey (multiple answers were allowed)

on BAD was 23%, with a significantly different rate of up to 42% of respondents with $^{75}\text{SeHCAAT}$ availability ($p < 0.001$). Almost all participants claimed the need for updates on BAD.

Discussion

The present survey investigated the knowledge and clinical attitudes of a group of Italian physicians in the management of BAD aiming to highlight the current clinical practice and guide future updates on this topic to increase awareness of this condition. To the best of our knowledge, only a previous survey was published on this topic [14]. It was carried out in the UK, including a small group of selected experts in this field ($n = 21$) and it was focused on improving diagnostic rates and management of BAD through a consensus on specific clinical cases. Therefore, the results are not fully comparable to our experience.

In our study we included a heterogeneous sample of physician and compared the answers from gastroenterologist to those of the remaining participant in the survey, which were mainly internal medicine doctors or surgeons. These medical specializations represent the three major types of physicians possibly facing this disease in their clinical practice. Although about half of the participants were from Northern Italy, where there is the greatest availability of

$^{75}\text{SeHCAAT}$ test in Italy, we surprisingly found no differences in $^{75}\text{SeHCAAT}$ availability among the two groups.

A considerable lack of knowledge was found among gastroenterologists and other physicians with an interest in digestive diseases. Only one-third of respondents correctly estimate the actual burden of BAD. Since the prevalence of chronic diarrhea in the general population has been estimated at around 5% and BAD is responsible for 26–50% of these cases [2, 21], BAD prevalence can be estimated to affect around 1% of the general population. When patients with IBS-D are considered, this rate increases up to 28.1%, according to a meta-analysis including more than 900 patients [4]. Therefore, about half of our respondents underestimated the burden of BAD. Surprisingly, despite the higher number of visits made by gastroenterologists for patients with chronic diarrhea, the rate of BAD diagnosis was comparable between gastroenterologists and other physicians. This can be explained by a selection bias of participants with a specific interest in these topics. The most commonly reported clinical criteria for BAD diagnosis were the presence of watery stools, > 3 CSBM/day, and the exclusion of organic/drug-related diseases. This finding is in keeping with what was reported in the survey by Walters et al. since the experts reported loose stools and frequency greater than 3 times/day as common findings [14]. However, the recently published Canadian guidelines for BAD management [16] suggested against using symptom presentation

for the initial assessment to identify patients with possible BAD, while recommending using risk factors (history of terminal ileal resection, cholecystectomy, or abdominal radiotherapy) for the initial assessment of patients with chronic non-bloody diarrhea. Most of the participants in our survey reported using ⁷⁵SeHCAT as a gold standard method for BAD diagnosis, when available, in line with international guidelines [6, 16]. Our data underline that the prescription of ⁷⁵SeHCAT in clinical practice, the perceived accuracy of this test, and the general awareness and knowledge of BAD are directly correlated with ⁷⁵SeHCAT test availability in the place of origin. On this line and supporting the importance of ⁷⁵SeHCAT availability, we found no difference in the number of ⁷⁵SeHCAT prescribed by gastroenterologists and other physicians operating in the same area.

The variation in ⁷⁵SeHCAT utilization among physicians likely reflects differences in local test availability, institutional protocols, and physician familiarity with BAD. In regions where the test is not accessible, clinicians may rely more on empirical therapy or alternative diagnostic approaches, leading to inconsistent practices [1]. This inconsistency underscores the need for standardized diagnostic pathways and wider dissemination of guideline-based approaches [14].

When the response to a cholestyramine trial was used as an ex adjuvantibus diagnosis, respondents heterogeneously reported using different doses of the drug. In BAD studies, cholestyramine was generally started at a low doses of 2 to 4 g/day and titrated based on response (maximum, 4–24 g/day) [16]. When cholestyramine trial duration was considered, the majority of interviewed gastroenterologists reported a trial of 28 days, while other physicians reported shorter durations. Heterogeneous duration of cholestyramine trial from 4 to 12 weeks have been published [22]. However, lack of response to cholestyramine does not constitute per se exclusion of BAD and there is very little evidence to determine the relative role of ⁷⁵SeHCAT testing versus using an empiric trial of BAST to make a diagnosis of BAD [22]. Therefore, in most guidelines, other factors were considered when making a recommendation for or against a diagnosis based on a cholestyramine trial [6, 16]. Despite evidence supporting the efficacy of bile acid sequestrants, treatment prescription remains suboptimal. Barriers such as perceived poor tolerability, side effects such as bloating or constipation, and uncertainties regarding dose optimization may deter clinicians from initiating therapy [12]. Patient-related concerns, including palatability and long-term adherence, may further complicate therapeutic decision-making [23].

About one out of five respondents among gastroenterologists and those with the ⁷⁵SeHCAT availability believed that 7α C4 or FGF19 are accurate enough for BAD diagnosis. However, although these tests may have a good specificity for identifying patients with moderate BAD

(⁷⁵SeHCAT < 10%), they have insufficient sensitivity as diagnostic tests to be used alone and they are not widely available [24].

Notably, no difference was found in the reported satisfaction among physicians regarding therapies available for BAD, with a rate of satisfaction of about 31–34%. Furthermore, all respondents reported efficacy of therapies for BAD of less than 30%. Indeed, besides the high rates of remissions reported for BASTs in observational studies [2, 25], the few placebo-controlled trials available did not show that colestyramine or colesevelam were superior to placebo regarding bowel movements, although secondary non-clinical outcomes improved [15, 26–28]. However, the response to cholestyramine may vary according to the BAD etiology and its degree of severity. A metaanalysis published in 2009 reported that in the pooled data from 15 studies there was a correlation between the severity of malabsorption and response to BAST: response to colestyramine occurred in 96% of patients with < 5% retention, 80% at < 10% retention and 70% at < 15% retention [2]. Long-term efficacy of BASTs may be hampered by several factors, such as uncertainty on the optimal dose to be used, different individual responses, side effects such as bloating and constipation, vitamin and concomitant drug malabsorption [23]. Colesevelam seems to gain some therapeutic response in BAD in patients nonrespondent to cholestyramine according to a trial published in 2015, where colestyramine was unsuccessful in 44% of cases, 47% of which responded to colesevelam [29]. Recently, a diagnostic and therapeutic RCTs assessing C4 accuracy vs ⁷⁵SeHCAT and the therapeutic response to colesevelam found that colesevelam was superior to placebo at inducing remission of BAD diagnosed with C4 concentration greater than 46 ng/mL [30]. Secondary outcome data suggested similar efficacy in treating ⁷⁵SeHCAT-defined BAD [30].

Finally, we found that more than half of the participants were not satisfied with their own knowledge of BAD and this gap significantly increased when ⁷⁵SeHCAT test was not available in the place of origin. Almost all participants reported the need for updates on this condition. These findings suggest a critical need for targeted educational initiatives and broader access to diagnostic tools to reduce disparities in care [16, 22].

Our study has some limitations: first, the sample size was rather low leading to a possible error type II when performing comparison among groups, although the response rate was satisfying. Second, the overall knowledge of BAD may have been positively influenced by a selection bias, since most gastroenterologists and other physicians participating in the meeting expressed an interest in gastroenterological diseases. Also, it was not possible to use validated questionnaires or to use questions with pre-validated scales in order to explore BAD knowledge and management, thus

influencing the reliability of our questions. Furthermore, some heterogeneity in our results may be influenced by the different training and clinical experience. However, our survey also has several strengths: it is the first report describing the knowledge and awareness of BAD in Italy and more generally in a European country among practicing physicians. These data may be used in the future to improve the awareness and knowledge of this condition, e.g. with focused updating courses. Moreover, we provided real-life data regarding the current epidemiology and management of patients with BAD in Italy according to tests and drugs availability, and its burden on healthcare resources.

In conclusion, BAD is a common condition with a multifaceted etiology. At least one-third of patients with IBS suffer from this condition. 75SeHCAT testing is the gold standard method for the diagnosis of BAD, although available only in a few Italian centers. 75SeHCAT availability influences the awareness and knowledge of this disease, possibly leading to a faster diagnosis and consequently reducing the burden of this disease for the patient and healthcare facilities. Therapies currently available for the treatment of BAD are often not able to guarantee adequate symptom relief. Updates on BAD are needed to fill in this knowledge gap, especially in geographic areas where 75SeHCAT is not available.

Acknowledgements Thanks to Emanuela Crescini for Coordinating.

Funding Open access funding provided by Alma Mater Studiorum - Università di Bologna within the CRUI-CARE Agreement. This work was supported by Messaggi International Publisher & Events srl, Milan, Italy.

Data availability The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Conflict of interest Annibale B: Alfasiigma, Aboca. Barbara G: Aboca, Ab Biotics, Agave, Alfasiigma, Ag Pharma, Bayer, Biocodex, Boheringer, Bromatech, Cadigroup, Danone, Diadema, Falk Pharma, Ge Healthcare, Giuliani, Mayoly, Malesci, Monteresearch, Sanofi, Sofar, Yakult. Bellini M: Alfasiigma, Diadema, Agave, Ferring, Ag Pharma, Bromatech, Sila, Depofarma. Cammarota G: Aurora Biopharma, Delta Pharma. Corazziari ES: Aboca spa, Sofar spa, Alfasiigma spa, GE Healthcare. Fries W: Abbvie, Pfizer, Janssen, Galapagos. Marasco G: Aboca, AgPharma, AlfaSigma, Bayer, Bromatech, CINECA, Clorofilla, Coreresearch, Echosens, EG Pharma, Eli Lilly, Ferring, Giuliani, Malesci, Mayoly Spindler, Menarini, Monteresearch, Named, Noos, Galenika, Recordati, Schwabe Pharma, Unifarco. Portincasa P: Aboca, Allergosan, Omega Pharma. Stanghellini V: Alfasiigma, Bayer, Bromatech, Ge Healthcare. Usai Satta P: Alfasiigma. Benedetti A declares no conflict of interest.

Human and animal rights statement and Informed consent The present survey investigated knowledge about the management of BAD in a group of Italian physicians without any involvement of patients. All physicians provided electronic informed consent before participation,

and data were collected anonymously. The study was deemed exempt from ethics approval.

Open Access This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by/4.0/>.

References

- Vijayvargiya P, Camilleri M (2019) Current practice in the diagnosis of bile acid diarrhea. *Gastroenterology* 156:1233–1238. <https://doi.org/10.1053/j.gastro.2018.11.069>
- Wedlake L, A'Hern R, Russell D et al (2009) Systematic review: the prevalence of idiopathic bile acid malabsorption as diagnosed by SeHCAT scanning in patients with diarrhoea-predominant irritable bowel syndrome. *Aliment Pharmacol Ther* 30:707–717. <https://doi.org/10.1111/j.1365-2036.2009.04081.x>
- Walters JRF (2010) Defining primary bile acid diarrhea: making the diagnosis and recognizing the disorder. *Expert Rev Gastroenterol Hepatol* 4:561–567. <https://doi.org/10.1586/egh.10.54>
- Slaterry SA, Niaz O, Aziz Q et al (2015) Systematic review with meta-analysis: the prevalence of bile acid malabsorption in the irritable bowel syndrome with diarrhoea. *Aliment Pharmacol Ther* 42:3–11
- Barbara G, Cremon C, Bellini M et al (2023) Italian guidelines for the management of irritable bowel syndrome: joint consensus from the Italian Societies of: Gastroenterology and Endoscopy (SIGE), Neurogastroenterology and Motility (SINGEM), Hospital Gastroenterologists and Endoscopists (AIGO), Digestive Endoscopy (SIED), General Medicine (SIMG), Gastroenterology, Hepatology and Pediatric Nutrition (SIGENP) and Pediatrics (SIP). *Dig Liver Dis* 55:187–207. <https://doi.org/10.1016/J.DLD.2022.11.015>
- Savarino E, Zingone F, Barberio B et al (2022) Functional bowel disorders with diarrhoea: clinical guidelines of the United European Gastroenterology and European Society for Neurogastroenterology and Motility. *United Eur Gastroenterol J*. <https://doi.org/10.1002/UEG2.12259>
- Marasco G, Cremon C, Barbaro MR et al (2022) Pathophysiology and clinical management of bile acid diarrhea. *J Clin Med*. <https://doi.org/10.3390/jcm11113102>
- Mekjian HS, Phillips SF, Hofmann AF (1971) Colonic secretion of water and electrolytes induced by bile acids: perfusion studies in man. *J Clin Invest* 50:1569–1577. <https://doi.org/10.1172/jci106644>
- McJunkin B, Fromm H, Sarva RPAP (1981) Factors in the mechanism of diarrhea in bile acid malabsorption: fecal pH – a key determinant. *Gastroenterology* 80:1454–1464
- Pattni S, Walters JRF (2009) Recent advances in the understanding of bile acid malabsorption. *Br Med Bull* 92:79–93. <https://doi.org/10.1093/bmb/ldp032>
- Bannaga A, Kelman L, O'connor M et al (2017) How bad is bile acid diarrhoea: an online survey of patient-reported symptoms

- and outcomes. *BMJ Open Gastroenterol* 4:1–6. <https://doi.org/10.1136/bmjgast-2016-000116>
12. Mottacki N, Simrén M, Bajor A (2016) Review article: bile acid diarrhoea – pathogenesis, diagnosis and management. *Aliment Pharmacol Ther* 43:884–898. <https://doi.org/10.1111/apt.13570>
 13. Balzer K, Breuer N, Quebe-Fehling E (1993) Postprandial serum bile acid level and ⁷⁵SeHCAT retention in diagnosis of bile acid malabsorption syndrome. a comparative study. *Med Klin (Munich)* 88(Suppl 1):23–28
 14. Walters JRF, Arasaradnam R, Andreyev HJN (2020) Diagnosis and management of bile acid diarrhoea: a survey of UK expert opinion and practice. *Frontline Gastroenterol* 11:358–363. <https://doi.org/10.1136/flgastro-2019-101301>
 15. Vijayvargiya P, Camilleri M, Carlson P et al (2020) Effects of colestevlam on bowel symptoms, biomarkers, and colonic mucosal gene expression in patients with bile acid diarrhea in a randomized trial. *Clin Gastroenterol Hepatol* 18:2962–2970.e6. <https://doi.org/10.1016/j.cgh.2020.02.027>
 16. Sadowski DC, Camilleri M, Chey WD et al (2020) Canadian association of gastroenterology clinical practice guideline on the management of bile acid diarrhea. *Clin Gastroenterol Hepatol* 18:24–41.e1. <https://doi.org/10.1016/j.cgh.2019.08.062>
 17. Battat R, Duijvestein M, Vande Casteele N et al (2019) Serum concentrations of 7 α -hydroxy-4-cholesten-3-one are associated with bile acid diarrhea in patients with Crohn's disease. *Clin Gastroenterol Hepatol* 17:2722–2730.e4. <https://doi.org/10.1016/j.cgh.2018.11.012>
 18. Borup C, Syversen C, Bouchelouche P et al (2015) Diagnosis of bile acid diarrhoea by fasting and postprandial measurements of fibroblast growth factor 19. *Eur J Gastroenterol Hepatol* 27:1399–1402. <https://doi.org/10.1097/MEG.0000000000000476>
 19. Shrank WH, Rogstad TL, Parekh N (2019) Waste in the US health care system: estimated costs and potential for savings. *J Am Med Assoc* 322:1501–1509. <https://doi.org/10.1001/jama.2019.13978>
 20. Hiatt JG, Shamsie SG, Schectman G (1999) Discontinuation rates of cholesterol-lowering medications: implications for primary care. *Am J Manag Care* 5:437–444
 21. Gracie DJ, Kane JS, Mumtaz S et al (2012) Prevalence of, and predictors of, bile acid malabsorption in outpatients with chronic diarrhea. *Neurogastroenterol Motil* 24:983–990. <https://doi.org/10.1111/j.1365-2982.2012.01953.x>
 22. Farrugia A, Arasaradnam R, Ramesh Arasaradnam P (2021) Bile acid diarrhoea: pathophysiology, diagnosis and management. *Frontline Gastroenterol* 12:500–507. <https://doi.org/10.1136/FLGASTRO-2020-101436>
 23. Walters JRF, Pattni SS (2010) Managing bile acid diarrhoea. *Therap Adv Gastroenterol* 3:349–357. <https://doi.org/10.1177/1756283X10377126>
 24. Camilleri M, Nurko S (2022) Bile acid diarrhea in adults and adolescents. *Neurogastroenterol Motil* 34:e14287. <https://doi.org/10.1111/NMO.14287>
 25. Wielandt TO, Møller EH, Krag E (1985) Effect of enterocoated cholestyramine on bowel habit after ileal resection: a double blind crossover study. *Br Med J (Clin Res Ed)* 290:1315. <https://doi.org/10.1136/bmj.290.6478.1315>
 26. Fernández-Bañares F, Rosinach M, Piqueras M et al (2015) Randomised clinical trial: colestyramine vs. hydroxypropyl cellulose in patients with functional chronic watery diarrhoea. *Aliment Pharmacol Ther* 41:1132–1140. <https://doi.org/10.1111/apt.13193>
 27. Beigel F, Teich N, Howaldt S et al (2014) Colesevelam for the treatment of bile acid malabsorption-associated diarrhea in patients with Crohn's disease: a randomized, double-blind, placebo-controlled study. *J Crohns Colitis* 8:1471–1479. <https://doi.org/10.1016/j.crohns.2014.05.009>
 28. Appleby RN, Bajor A, Gillberg PG et al (2017) Effects of conventional and a novel colonic-release bile acid sequestrant, A3384, on fibroblast growth factor 19 and bile acid metabolism in healthy volunteers and patients with bile acid diarrhoea. *United Eur Gastroenterol J* 5:380–388. <https://doi.org/10.1177/2050640616662432>
 29. Orekoya O, McLaughlin J, Leitao E et al (2015) Quantifying bile acid malabsorption helps predict response and tailor sequestrant therapy. *Clin Med* 15:252–257. <https://doi.org/10.7861/clinmedicine.15-3-252>
 30. Borup C, Vinter-Jensen L, Jørgensen SPG et al (2023) Efficacy and safety of colestevlam for the treatment of bile acid diarrhoea: a double-blind, randomised, placebo-controlled, phase 4 clinical trial. *Lancet Gastroenterol Hepatol* 8:321–331. [https://doi.org/10.1016/S2468-1253\(22\)00401-0](https://doi.org/10.1016/S2468-1253(22)00401-0)

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.