Title

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ORIGINAL ARTICLE

Impact of Pruritus on Quality of Life and Current Treatment Patterns in Patients with Primary Biliary Cholangitis

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Abstract

Background and Aims Patients with primary biliary cholangitis (PBC) often suffer with pruritus. We describe the impact of pruritus on quality of life and how it is managed in a real-world cohort.

Methods TARGET-PBC is a longitudinal observational cohort of patients with PBC across the USA. Data include information from medical records for three years prior to the date of consent up to 5 years of follow-up. Enrolled patients were asked to complete patient-reported outcome surveys: PBC-40, 5-D itch, and the PROMIS fatigue survey. Kruskal–Wallis tests were used to compare differences in symptoms between groups.

Results A total of 211 patients with completed PRO surveys were included in the current study. PRO respondents were compared with non-respondents in the TARGET-PBC population and were broadly similar. Pruritus was reported in 170 patients (81%), with those reporting clinically significant pruritus (30%) scoring worse across each domain of the PBC-40 and 5-D itch, more frequently having cirrhosis, and having significantly greater levels of fatigue. Patients reporting clinically significant pruritus were more likely to receive treatment, but 33% had never received treatment (no itch = 43.9%, mild itch = 38.3%).

Conclusions The prevalence of pruritus was high in this population, and those reporting clinically significant pruritus had a higher likelihood of having advanced disease and worse quality of life. However, this study found that pruritus in PBC is under-treated. This may be due in part to ineffectiveness of current treatments, poor tolerance, or the lack of FDA-approved medications for pruritus.

Keywords Primary Biliary Cholangitis · Real-world evidence · Pruritus · Treatment

Abbreviations

PBC	Primary Biliary Cholangitis
AASLD	American Association for the Study of Liver Disease
EASL	European Association for the Study of the Liver
QOL	Quality of Life
PRO	Patient-reported outcome
CS	Clinically significant
IQR	Interquartile range
AMA	Antimitochondrial antibody
UDCA	Ursodeoxycholic acid

TARGET-PBC Investigators – see Appendix for complete list.

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Background

Primary biliary cholangitis (PBC) is a chronic cholestatic liver disease with debilitating symptoms, including pruritus and fatigue. Recent large clinical trials have found a baseline prevalence of pruritus in patients with PBC of about 50–70% [1, 2]. Other studies from the UK have shown a significant impact of these symptoms on quality of life [3, 4]. However, an understanding of the impact of pruritus in PBC in the real world, particularly within the USA, is lacking. Multiple potential therapies for cholestatic pruritus have been studied and found to be partially effective, including cholestyramine, rifampicin, naltrexone, and sertraline, but none are FDA-approved for use to treat pruritus in PBC patients specifically. The American Association for the Study of Liver Disease (AASLD) and European Association for the Study of the Liver (EASL) recommend a step-wise

approach to treat pruritus in PBC,[5, 6], but the extent of uptake of these recommendations in the medical community is also unknown. This study characterizes the population with pruritus in the TARGET-PBC cohort. The purpose is to describe the population characteristics, the impact of pruritus on quality of life (QOL), and the management practice of pruritus in a real-world cohort.

Patient Cohort

TARGET-PBC is a longitudinal observational cohort of patients with PBC receiving usual care in hepatology or gastroenterology clinics at one of 38 academic and community sites across the USA. The design and a description of the cohort have been presented in more detail elsewhere [7]. Patients with a diagnosis of PBC by a treating physician were eligible for inclusion in the study. Individuals actively enrolled in a clinical trial were excluded.

Methods

Following informed consent, patient data were obtained from both medical records and patient self-report. Medical records for each patient included three years prior to the date of consent and up to five years prospectively. Data were abstracted from the medical records, including clinical notes, laboratory data, medication lists, all prior imaging reports, radiographic and other diagnostic procedures, and all prior liver biopsy reports. Missing data were minimized by performing site queries. In addition to clinical and treatment data, patients were asked to complete patient-reported outcome (PRO) surveys approximately every six months. These PRO surveys included the PBC-40, 5-D Itch, and the PROMIS fatigue survey, described below. The concepts covered by the PRO questions are summarized in Table 1.

Target RWE is the sponsor of TARGET-PBC and is responsible for the data and quality control activities. Data are abstracted from complete medical records which are uploaded into the database by sites for enrolled participants. There are various processes in place to ensure the quality of data collected for the TARGET-PBC study. Edit checks, auto-coding of adverse events and concomitant medications, expert adjudication, and source-document verification are all components of the data quality system.

The analysis reported here focuses on the population who had completed PROs at least once and uses the most recent PRO, clinical and laboratory data. The medication list was developed as of the last medical record abstraction and includes all recorded medications that a patient had been prescribed for PBC and associated cholestatic pruritus.

Patient Reported Outcome (PRO) Surveys

The PBC-40 consists of 40 questions across six domains of interest related to PBC: general symptoms, itch, fatigue,

Table 1 Patient reported outcome (PRO) survey descriptions

Survey	General topics of questions
PBC- 40	
Itch	Scratching until skin is raw, embarrassment from itch, sleep disturbance from itch
Fatigue	Difficulty getting out of bed, early bedtime, daytime sleepiness difficulty completing daily activities, having to pace activities, needing time to recover, feeling worn out, drained
General Symptoms	Dry eyes/mouth, aching arms/legs, bloating, right sided discomfort
Cognition	Memory, concentration
Social	Isolation, guilt, neglect, impaired sex life
Emotional	Stress, worry, feeling down
5-D Itch	
Degree	Intensity of itch
Duration	Hours per day of itching
Disability	Impact of itch on sleep, social, and work activities
Direction	Whether itch is improving or worsening
Distribution	Number of body parts affected by itch
PROMIS Fatigue	
Frequency Duration Intensity Physical Mental Social	Mild feelings of tiredness to an overwhelming, debilitating and sustained sense of exhaustion that decreases the ability to execute daily activities and function normally in family or social roles

cognition, social, and emotional [8]. Items are scored from zero or one to five and individual item scores are combined to give a total domain score. This questionnaire assesses symptoms over the last 4 weeks. Using the threshold for clinical significance suggested by the developers, clinically significant (CS) itch was defined as ≥ 7 points from a maximum of 15 on the itch domain and mild itch as ≥ 1 and < 7.

The 5-D Itch scale comprises five domains: duration, degree, direction, disability, and distribution [9], with each domain accounting for 5 points. The domain scores are then added together for a total 5-D score, potentially ranging from 5 (no pruritus) to 25 (most severe pruritus). This survey assesses itch over the last 14 days.

The PROMIS fatigue survey (PROMIS Item Bank v1.0-Short Form 8a) evaluates symptoms ranging from a mild subjective tiredness to an overwhelming, debilitating, and sustained sense of exhaustion [10]. The domains include fatigue (frequency, duration, and intensity) and the impact of fatigue (on physical, mental, and social activities). This survey asks patients to rate average fatigue over the past 7 days using a five-point Likert scale from 1 to 5, where 1 means the least impact/severity, and 5 being the most. The total scores for all items are added [total of 8 to 40] and cross-referenced with a lookup table to obtain a T-Score.

Statistical Methods

Descriptive statistics were reported for continuous and categorical variables overall and by itch severity. Continuous variables were summarized using the frequency, median, minimum, maximum, and interquartile range (IQR) values. Categorical variables were summarized using the frequency and the percentage relative to those with non-missing values. Kruskal–Wallis tests were used to compare median differences in symptoms between the mild and CS itch groups (no itch was excluded). Patient characteristics, disease severity, and treatment patterns were compared according to the presence and severity of itching. All analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA).

Results

Subject Characteristics

A total of 211 out of 671 PBC patients completed PROs allowing the presence (or absence) and severity of itch to be assessed and were included in the current study. Table 2 shows the characteristics of patients who responded compared to those who opted not to complete the PROs. No obvious demographic differences were observed between these groups except that respondents were more likely to be white/non-Hispanic/Latino ($p = 0.01$) and have a lower GLOBE score ($p < 0.05$). PBC patients were of a similar age at the time of the survey (respondents–61; non-respondents–63) and had been diagnosed with PBC a similar amount of time (respondents–7.2 years; non-respondents -5.6 years). Patients were predominantly female (respondents–92%; non-respondents–91%), white (respondents–87%; non-respondents–79%), and non-Hispanic (respondents–84%; non-respondents–75%). Patients frequently had Antimitochondrial antibody (AMA) positivity documented (respondents–87%; non-respondents–81%) and had undergone a liver biopsy (respondents–66%; non-respondents–60%). Under half of patients had cirrhosis (respondents–35%; non-respondents –41%). Of the 211 patients within the study, 83% received care from an academic site, while the remaining patients received care at a community site.

PBC-40

Itch Domain

The presence of itching of any degree was reported in 170 (81%) patients. The majority of these, 107 (63%) had a mild itch, and 63 (37%) were classified as having a clinically significant itch with a score ≥ 7. Patients with CS itch were younger (CS = 58 y/o; mild itch = 64 y/o; no itch = 64 y/o), more frequently had cirrhosis (CS = 48% vs. mild itch = 27%, and no itch = 37% $p = 0.03$) and had higher alkaline phosphatase levels (CS = 177 IU/L vs. mild itch = 143 IU/L and no itch = 153 IU/L, $p = 0.002$) compared to those with mild or no itch, respectively (Table 3). P-values in Table 3 are tests for any difference between the three groups (CS itch, mild itch, and no itch).

Other Domains

Across all domains of the PBC-40, those with CS itch scored significantly worse than those with mild itch. There was no notable difference in scores between those with mild itch and those with no itch. The largest difference was seen in cognitive and social domains; median scores in the CS itch group were ~ 80% higher than those in the no itch group, indicating more distress in patients with CS itch. In other domains—fatigue, symptoms, and emotional—the difference was smaller, though still substantial, with median scores 42%, 46%, and 50% greater, respectively, for the CS itch group (Fig. 1).

5-D Itch

The scores for the 5-D Itch Scale were consistent with the PBC-40 itch domain. Respondents with CS itch scored significantly higher (worse) than those with mild itch across all domains (Fig. 2). The direction domain assesses

Table 2 Demographics of PRO survey respondents vs. non-respondents

	Respondents (n = 211)	Non-Respondents (n = 460)	*p* value
Gender			
n	211	460	0.6461
Female	194 (91.9)	418 (90.9)	
Age at study entry (years)			
Median (n)	60 (211)	62 (459)	0.5179
Q1 – Q3	52–69	53–70	
Age at diagnosis (years)			
Median (n)	52 (208)	53 (439)	0.1305
Q1–Q3	44–58	45–61	
Current age (years)			
Median (n)	61 (211)	63 (459)	0.5849
Q1–Q3	54–70	54–71	
Race, n (%)			
n	211	460	0.0124
White	184 (87.2)	362 (78.7)	
Black or African American	6 (2.8)	30 (6.5)	
American Indian or Alaska Native	0 (0)	8 (1.7)	
Asian	2 (0.9)	14 (3.0)	
Other	5 (2.4)	15 (3.3)	
Not reported	14 (6.6)	31 (6.7)	
Ethnicity, n (%)			
n	211	460	0.0289
Not Hispanic or Latino	177 (83.9)	347 (75.4)	
Hispanic or Latino	18 (8.5)	92 (20.0)	
Other	15 (7.1)	19 (4.1)	
Not Reported	1 (0.5)	2 (0.4)	
Duration of PBC at enrollment (years)			
Median (n)	7.2 (208)	5.6 (439)	0.1494
Q1–Q3	3.3–14.3	2.8–12.1	
Duration of pruritus from onset to enrollment (years)			
Median (n)	1.8 (142)	2.0 (278)	0.7529
Q1–Q3	0.5–2.9	0.8–2.8	
Most recent ALP result (IU/L)			
Median (n)	150 (210)	166 (456)	0.7012
Q1–Q3	124–211	120–228	
Most recent total bilirubin (mg/dL)			
Median (n)	0.6 (210)	0.6 (454)	0.2254
Q1–Q3	0.4–0.9	0.4–1.0	
Cirrhosis			
N	211	460	0.1670
Yes, n (%)	74 (35.1)	187 (40.7)	
Decompensated cirrhosis			
N	74	187	0.0081
Yes, n (%)	30 (40.5)	105 (56.1)	
Biopsy			
N	211	460	0.1440
Yes, n (%)	139 (65.9)	276 (60.0)	
Most recent globe score			
Median (n)	– 0.6 (198)	– 0.4 (434)	0.0170
Q1–Q3	– 1.1–0.2	– 1.0–0.6	

Table 2 (continued)

	Respondents (n = 211)	Non-Respondents (n = 460)	*p* value
Most recent child–pugh score			
Median (n)	5.0 (131)	5.0 (316)	0.0204
Q1–Q3	5.0–6.0	5.0–7.0	
AMA Status, n (%)			
N	180	379	0.0524
AMA Negative	23 (12.8%)	73 (19.3%)	
AMA Positive	157 (87.2%)	306 (80.7%)	

ALP Alkaline Phosphatase, *AMA* Anti-mitochondrial antibody

Table 3 Patient Characteristics by PBC-40 Itch Severity

	= 0 No itch	> = 1 to < 7 Mild itch	> = 7 Clinically significant itch	P-value[†]
All Patients, n (%)	41 (19)	107 (51)	63 (30)	0.844
Gender Female, n (%)	38 (93)	97 (91)	59 (94)	
Current age (years)				
Median (Q1–Q3)	64 (56–71)	64 (55–71)	58 (52–64)	0.0124
Age at diagnosis (years)				
Median (Q1–Q3)	52 (42–59)	54 (46–60)	49 (39–56)	0.0398
Most recent ALP (IU/L)				
Median (Q1–Q3)	153 (126–228)	143 (116–187)	177 (133–284)	0.0019
Most recent total bilirubin (mg/dl)				
Median (Q1-Q3)	0.5 (0.4–0.8)	0.6 (0.4–0.8)	0.8 (0.5 – 1.2)	0.0007
Cirrhosis n (%)	15 (37)	29 (27)	30 (48)	0.0277
Decompensated Cirrhosis				
N	15	29	30	
Yes, n (%)	5 (33)	7 (24)	18 (60)	0.0174

ALP Alkaline phosphatase

[†]*P* values are tests for any difference between the three groups (CS itch, mild itch, and no itch)

whether itching has gotten better/worse, and both groups scored similarly. Patients with CS itch had a mean duration of itch of less than 6 h per day (although ~ 20% of those with CS itch reported experiencing more than 12 h itching per day) that involved an average of six to 10 body parts, and patients with CS itch reported more widespread itch than those with mild itch, ~ 70% reporting itch affecting > 6 body parts compared with < 20% of those with mild itch. The most commonly reported body parts affected by itch were: head/scalp 67%, lower legs 63%, back 62%, palms of hands 43%, and soles of feet 35%; (data not shown). The majority reported an unchanged itch severity that for most is unchanged over the previous 2 weeks, with 19% reporting a worsening itch. Itch caused significant disability predominantly in sleep (88%), but also occasionally impacting patients' social life (58%), housework/errands (53%), and work/school (44%) (data not shown).

PROMIS Fatigue

Patients with CS itch reported significantly greater fatigue on the PROMIS fatigue instrument than those with mild and no itch. Individuals with CS itch reported the highest level of fatigue on the following items with a median score of four: "worn out, so tired I had to force myself to do things I needed to do, if I was busy one day I needed at least another day to recover, and I had to pace myself for day-to-day things." Median scores in the CS, mild and no itch groups were 61, 50 and 50, respectively ($p < 0.0001$ CS vs. Mild Itch) (Fig. 3).

Treatments for Pruritus

Overall, patients suffering from CS itch were more likely to receive treatment for itch than those with mild itch (51 vs 28%)

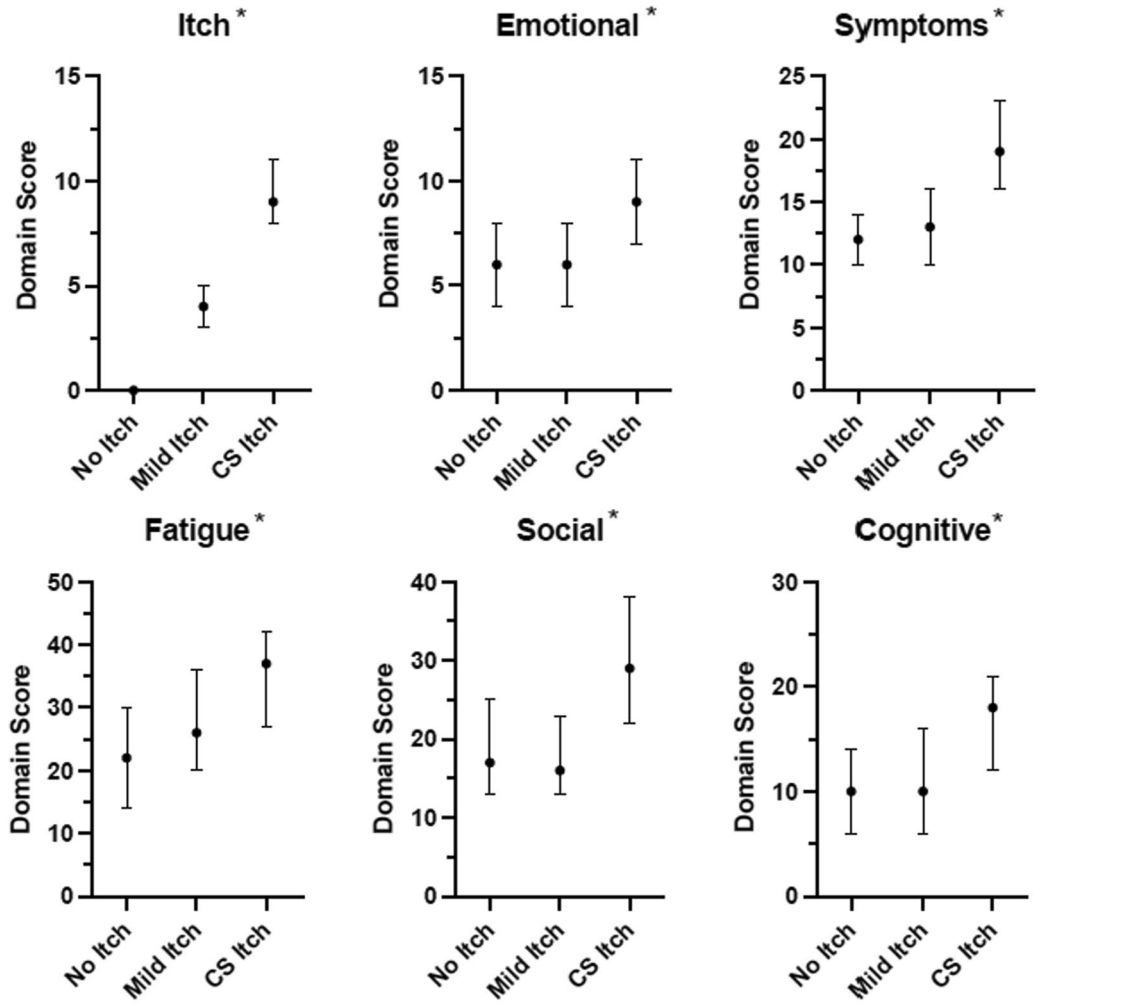
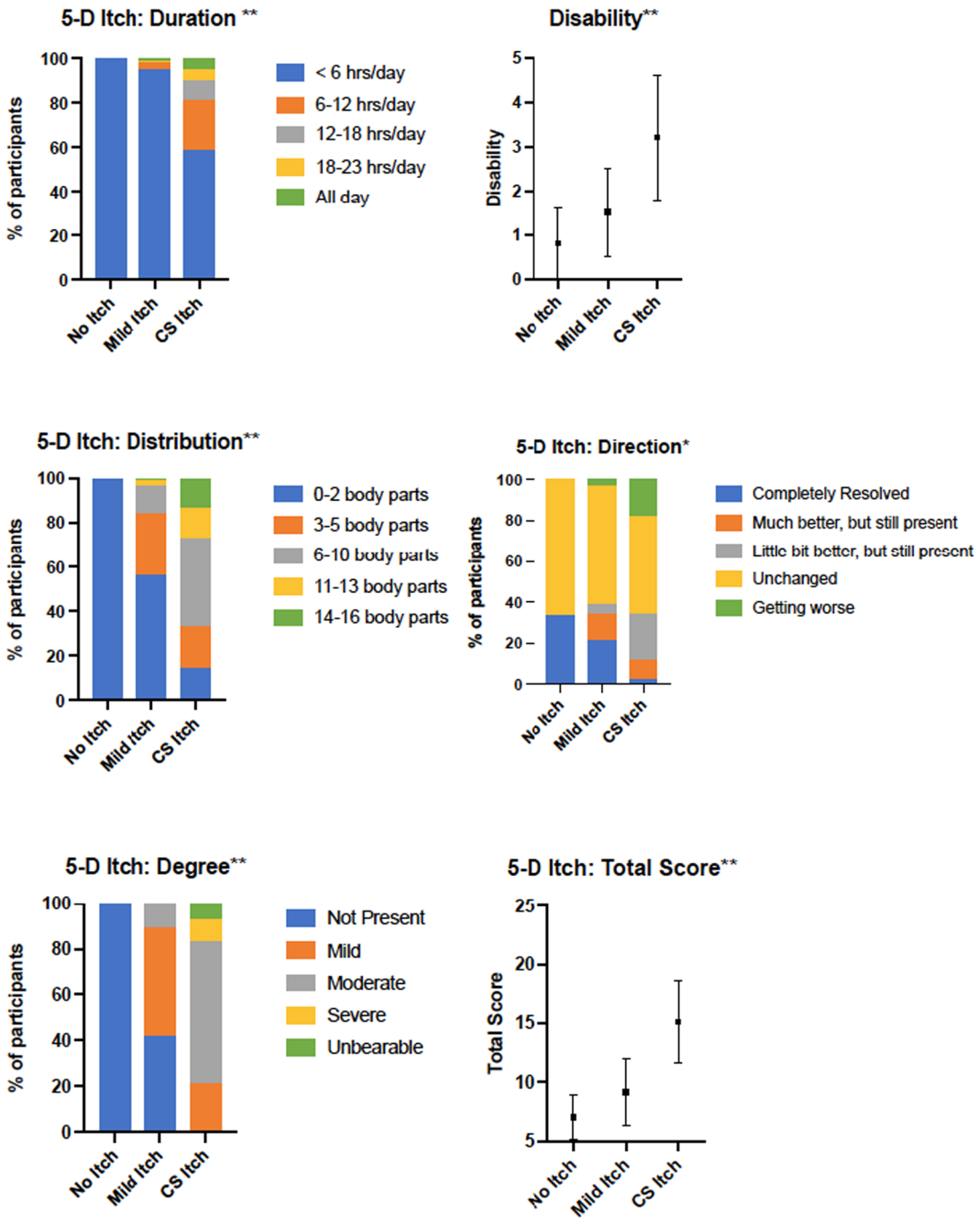


Fig. 1 Median and IQR PBC-40 domain scores by itch severity

(Table 4). However, based on their medical records, 33% of patients reporting CS itch had never received any treatment for itch. These same patients suffering from CS itch were more likely to currently have multiple treatments concomitantly for their underlying PBC documented in their medical record than those with mild itch (32 vs 22%) and to be taking fenofibrate (16%vs 1%). Nearly all patients (97%), regardless of severity of itch, were currently taking ursodeoxycholic acid (UDCA), either alone, or in combination with another medication, while only 16% had received OCA (as a combination or alone) (Fig. 4). Of those receiving pruritus treatment, the most common were antihistamines for both mild (73%) and CS itch (66%), followed by bile acid binding resins (23 and 25%, respectively) (Table 4). Patients with CS itch, as opposed to those with mild itch, were also more likely to have the following concomitant medications: lactulose (16%), spironolactone (15%), pantoprazole (14%), and ondansetron (12%). When examining treatment strategies at sites, patients treated at community sites received UDCA slightly more than those at academic sites (81%, n = 29; 71%, n = 124, respectively) and slightly less combinations of UDCA/OCA (17%, n = 6; 20%, n = 35, respectively) and UDCA/fenofibrate (3%, n = 1; 5%, n = 9, respectively).



Significance testing was conducted between Mild Itch and Clinically Significant (CS) Itch
*p-value <0.01
**p-value <0.0001
5-D Itch categories: Degree – intensity of itch, Duration – hours per day of itching, Disability – impact of itch on sleep, social, and work activities, Direction – whether itch is improving or worsening, Distribution – number of body parts affected by itch
†5-D Itch Disability and 5-D Itch Total Score display Mean (SD)

Fig. 2 5-D Itch domains by PBC-40itch severity

Discussion

These data from TARGET-PBC, a large, real-world US cohort, highlight the pervasive impact of pruritus in patients with PBC, as well as some shortcomings of the medical community's current response.

The overall prevalence of itch was high, with 81% of respondents reporting itch of any degree, and 37% reporting

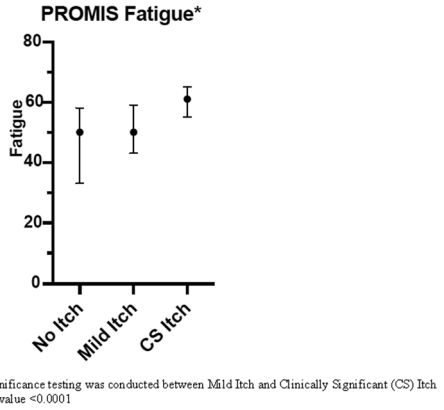


Fig. 3 Mediand and IQR PROMIS fatigue by PBC-40 itch severity

itch that was severe enough to be deemed "clinically significant" (CS) per PBC-40 scoring. Patients with CS itch were more likely to have advanced disease.

Simultaneous administration of 3 different PROs allowed for the assessment of both congruity and the measurement of the impact of PBC itch on quality of life. Notably, patients with CS itch scored significantly worse on all quality-of-life assessments when compared to those with mild or no itch. Clinically significant itch was associated with worse cognition, fatigue, emotional health, sleep, social life (including isolation, guilt, neglect, and sex life). The impact of itch on quality of life was truly pervasive, and over half had significant fatigue, cognitive, and other general symptom burden.

The association between itch and fatigue among patients with PBC has been previously examined. A study in 2010 focusing on fatigue in PBC showed that 66 patients (20%) indicated pruritus at the time of the administered questionnaire and this was associated with higher fatigue scores than those who did not report itch ($32.9 + 11.1$ versus $26.0 + 10.8$, $p < 0.001$) [11]. Itch and fatigue both directly impact a patient's overall quality of life, and it is extremely likely that itch can negatively influence the amount of fatigue a patient reports. Persistent pruritus has been found to impede sleep and lead to severe sleep deprivation [12].

This study found that pruritus in PBC is under-treated in clinical practice. Only half (50.8%) of patients with clinically significant itch were receiving treatment at the time of the surveys, and a third reported never receiving any medical treatment for itch. When itch medication was used, the step-wise guidelines put forth by specialty professional societies was not usually followed. In this cohort, 69.4% of patients with itch were currently treated with antihistamines, despite data that cholestatic itch is not histamine-mediated [13]. Only 24% of those with any itch who were receiving treatment for pruritus, and 9% all patients with any itch reported, were treated with bile acid binding resins, which are recommended as first-line therapy by both AASLD and EASL. Patients with CS itch were more likely to be taking fenofibrate; this may reflect their refractory disease, or the tendency of physicians to prefer fibrates in patients with itch since fibrates have been associated with improvement in itch [14–16]. However, it is perhaps surprising that despite treatment with fibrates these patients were still reporting CS itch.

A distinct advantage of these data is that they are derived from a broad, real-world collection of information, both retrospective and prospective. Clinical trial participants were excluded, and the 38 sites were diverse, including both community and academic centers across the USA. Ethnic diversity, while still limited, was increased compared to other PBC studies [17]. Although some selection bias may have occurred because not all enrolled subjects completed the PRO surveys, the percentage of respondents (31%) was good compared to most online survey response rates [18]. Whites were more than twice as likely to complete the PROs as compared to Blacks, Hispanics, and Asians. Survey respondents were also less likely to have advanced disease. By design, PROs were examined cross-sectionally based on availability of data and the treatment efforts were examined throughout the retrospective and prospective period in TARGET-PBC. However, there is a paucity of data examining PROs among patients with PBC in combination with comprehensive, robust data from medical records. These findings help provide a much needed examination into a patient's quality of life and how it relates to current and past treatment patterns.

Given that clinically significant itch was more often seen in patients with advanced disease, the potential selection bias of this study may have led to an underestimation of the true prevalence and impact of pruritus in the real world. The current study is also not able to elucidate the pathophysiology of cholestatic itching or prove a mechanistic cause and effect between itching and quality of life, but it clearly shows a disease severity-dependent, association. Additionally, OCA, as in the US label, might induce itch which could act as a potential confounder for reported pruritus among the subset of patients currently who were receiving OCA [19]. The study design presented here does not allow for investigating the proportion of patients whose itching started or worsened following the start of OCA and therefore should be investigated further. While TARGET RWE does have information regarding the dose of medication and frequency when it is available within the medical record, information was not obtained regarding patient compliance and the frequency of refills.

These eye-opening data illustrate the real-world extent, impact, and current management practice patterns of pruritus in PBC patients within the USA. Unfortunately, debilitating itch is prevalent but underappreciated, and current options for medical treatment are not fully utilized. We speculate this may be because current treatment options are only partially effective, poorly tolerated, and none are FDA-approved for

Table 4 Overall Treatment by Presence of Pruritus and by Pruritus Severity (on PBC 40 Itch Domain)

Summary	All	Itch Domain = 0 (No Itch)	Itch Domain > = 1 (Any Itch)	Itch Domain > = 1 to < 7 (Mild Itch)	Itch Domain > = 7 (CS Itch)
All participants, n (%)	211 (100)	41 (19.4)	170 (80.6)	107 (50.7)	63 (29.9)
Current PBC treatment, n (%)					
UDCA only	153 (72.5)	32 (78.0)	121 (71.2)	81 (75.7)	40 (63.5)
UDCA and OCA	41 (19.4)	7 (17.1)	34 (20.0)	23 (21.5)	11 (17.5)
UDCA and Fenofibrate	10 (4.7)	2 (4.9)	8 (4.7)	0 (0)	8 (12.7)
UDCA, OCA and Fenofibrate	1 (0.5)	0 (0)	1 (0.6)	0 (0)	1 (1.6)
OCA only	1 (0.5)	0 (0)	1 (0.6)	0 (0)	1 (1.6)
Fenofibrate only	2 (0.9)	0 (0)	2 (1.2)	1 (0.9)	1 (1.6)
Other	3 (1.4)	0 (0)	3 (1.8)	2 (1.9)	1 (1.6)
Current pruritus treatment					
Participants w/ current pruritus med, n (%)[†]	73 (34.6)	11 (26.8)	62 (36.5)	30 (28.0)	32 (50.8)
Participants w/ current pruritus med (Excl. OTC Antihist.)[‡], n (%)	38 (18.0)	1 (2.4)	37 (21.8)	13 (12.1)	24 (38.1)
Number of current pruritus medications					
Median (n)	1 (73)	1 (11)	1 (62)	1 (30)	1 (32)
Mean (SD)	1.2 (0.4)	1.0 (0.0)	1.2 (0.4)	1.1 (0.3)	1.3 (0.5)
Min–Max	1–3	1–1	1–3	1–2	1–3
Current pruritus medications[†]					
Ntihistamines	53 (72.6)	10 (90.9)	43 (69.4)	22 (73.3)	21 (65.6)
Bile acid binding resins	15 (20.5)	0 (0.0)	15 (24.2)	7 (23.3)	8 (25.0)
Rifampicin	4 (5.5)	0 (0.0)	4 (6.5)	0 (0.0)	4 (12.5)
Sertraline	7 (9.6)	1 (9.1)	6 (9.7)	1 (3.3)	5 (15.6)
Other	3 (4.1)	0 (0.0)	3 (4.8)	1 (3.3)	2 (6.3)
Pruritus treatments ever prescribed					
Participants ever taking pruritus medication, n (%)	101 (47.9)	18 (43.9)	83 (48.8)	41 (38.3)	42 (66.7)
Participants ever taking pruritus medication (excl. OTC antihist.), n (%)	60 (28.4)	4 (9.8)	56 (32.9)	19 (17.8)	37 (58.7)
Pruritus medications ever taken					
Antihistamines	74 (73.3)	16 (88.9)	58 (69.9)	31 (75.6)	27 (64.3)
Bile acid binding resins	31 (30.7)	3 (16.7)	28 (33.7)	9 (22.0)	19 (45.2)
Rifampicin	8 (7.9)	0 (0.0)	8 (9.6)	2 (4.9)	6 (14.3)
Sertraline	19 (18.8)	1 (5.6)	18 (21.7)	3 (7.3)	15 (35.7)
Other	10 (9.9)	1 (5.6)	9 (10.8)	3 (7.3)	6 (14.3)

CS Clinically significant, *UDCA* Ursodeoxycholic acid , *OCA* Obethicholic acid, *OTC* over the counter

[†]Current treatment is defined as at the last medical record abstraction

[‡]OTC Antihistamines include Cetirizine, Loratadine, Diphenhydramine, and Fexofenadine

treatment of cholestatic pruritus in patients with PBC specifically. Rigorously designed clinical trials, as well as greater research efforts, are needed to better evaluate and communicate the debilitating impact of pruritus in PBC patients and to identify highly effective therapies needed to provide effective solutions to this significant problem.

Key Points

For patients enrolled in TARGET-PBC, itching was examined to assess how a patient's quality of life was impacted. Patients who reported worse itch also reported worse

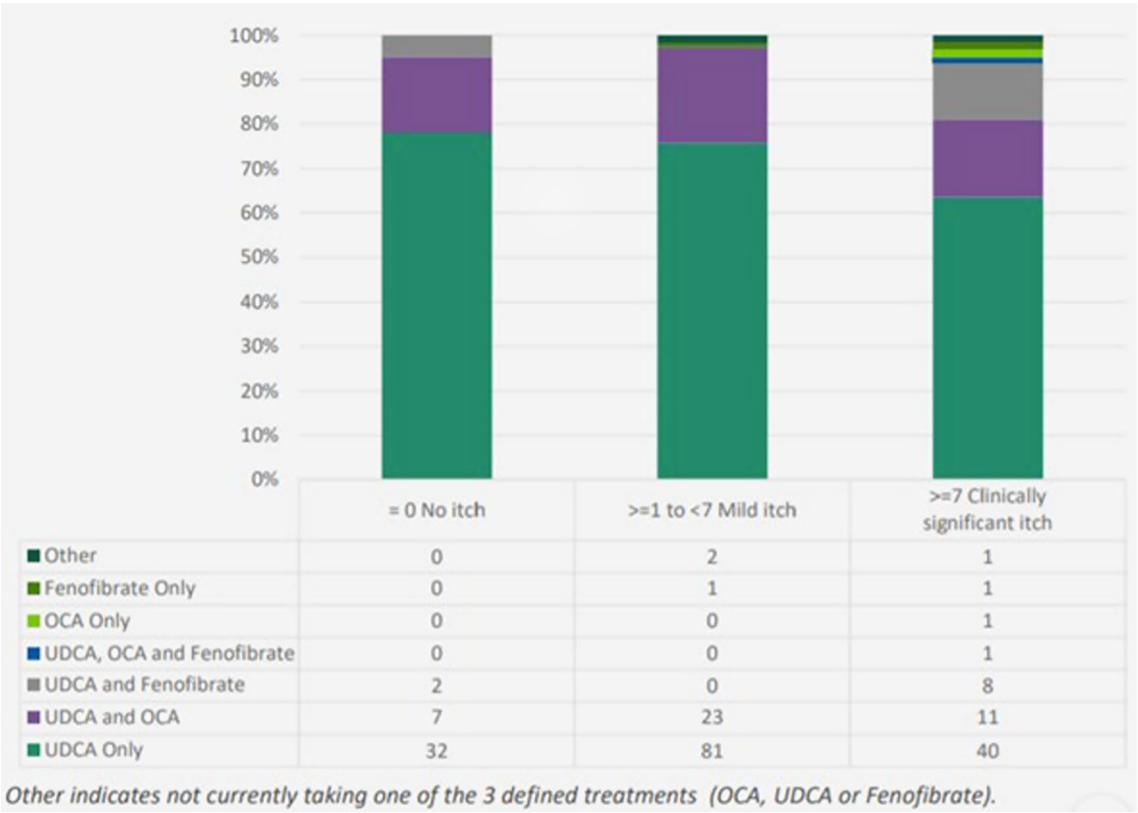


Fig. 4 Current PBC treatments

quality of life and more likely to be fatigued as measured by patient-reported surveys. Despite itching being a common problem among patients with PBC, it is not consistently treated with medications.

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Declarations

Conflict of interest MJM has research funding from TARGET PharmaSolutions, GlaxoSmithKline, Intercept Pharmaceuticals, CymaBay Pharmaceuticals, Genfit, Mirum, and Mallinckrodt; and consultation fees from TARGET PharmaSolutions, GlaxoSmithKline, CymaBay Pharmaceuticals, and Mallinckrodt. EC and WRK have no conflicts to report. HS and MM are employees of GlaxoSmithKline and hold stocks/shares in the company. AT was an employee of GSK at the time of the study and holds stocks/shares in the company. ARM, HLM, and RS are Target RWE employees. CB has research funding from Gilead Biosciences, Intercept Pharmaceuticals, CymaBay Pharmaceuticals, Takeda Pharmaceuticals, GlaxoSmithKline, BristolMyerSquibb, TARGET Pharmasolutions, Novartis, BiomX, Mirum, Genfit, Pliant, Cara Therapeutics, and Boston Scientific. CL has research funding from Gilead, Intercept, CymaBay, Genfit, GSK, Novartis, High Tide, Zydus, Cara Therapeutics, Mirum, Pliant, and Target PharmaSolutions; consultation fees from CymaBay, Genfit, GSK, Pliant, Mirum, Cara Therapeutics, Escient, Teva, Calliditas, and Intercept; royalties from Up-to-date; and is the Associate Editor for Hepatology, Member of the ABIM Test and Policy committee for transplant hepatology.

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