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CLINICAL REPORT

# Itch in Primary Biliary Cirrhosis: A Patients' Perspective

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**The perception of itch in primary biliary cirrhosis (PBC) is not characterized. Patients with primary biliary cirrhosis who were members of the PBCers Organization were invited to participate in an on-line survey addressing certain characteristics of their itch. Patients used their own words in the questions that asked for descriptions. A total of 238 subjects responded to the survey; of these, 231 were women, and 165 (69%) reported itch. One hundred and twenty-four patients from the 165 (75%) reported that itch preceded the diagnosis of primary biliary cirrhosis. A total of 58 from 164 (35%) respondents described their itch as "bugs crawling". Fifty-seven of 88 (64.7%) subjects reported that something cool relieved their itch, and 69 of 112 (61.6%) reported that heat worsened it. One hundred and seven of 164 (65.2%) respondents reported that the itch was worse at night. The most commonly prescribed medications were antihistamines and cholestyramine, and the most common type of medication reported as being associated with relief was antihistamine drugs. There was no systematic approach to the evaluation and treatment of itch in patients with primary biliary cirrhosis. Education on the subject of itch in primary biliary cirrhosis is warranted.** ***Key words: primary biliary cirrhosis; itch.***

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Primary biliary cirrhosis (PBC) is a liver disease of unknown etiology characterized by the presence of anti-mitochondrial antibodies in serum, chronic non-suppurative cholangitis on liver histology and cholestasis (1). Itch is the most common symptom associated with PBC. It has been reported to occur in 25–70% of patients with PBC (2). The itch of cholestasis, including that secondary to PBC, can be so severe that it is an indication for liver transplantation even in the absence of liver failure (3–5).

The negative impact of itch on the quality of life of patients with PBC is marked (3, 5–11); however, itch is difficult to describe and impossible to quantify subjectively (12). We hypothesized that by determining how patients with PBC experience their itch we would be able to identify specific characteristics of this symptom in PBC that might reveal some aspect of its pathophysiology, and that would provide information on how this symptom is managed nationwide.

## METHODS

The PBCers Organization is a non-profit organization that aims to provide education and support for family members and friends of people with PBC. Through the internet and other media it raises public awareness and the need for research into PBC. It also hosts conferences and fora to provide a support and communication network for patients with PBC.

The study was approved by the institutional review board of Columbia University, from where it was conducted. With the consent of the PBCers Organization, an icon for the survey was posted on their website (www.pbcers.org); patients were asked to sign an electronic consent form before participating in the study. The inclusion criteria for the survey were: (*i*) documented patient membership of the PBCers Organization (i.e. patients who have a diagnosis of PBC); and (*ii*) no prior liver transplant. Surveys were completed from June to September 2002. Questions were both multiple-choice and fill-ins, which allowed patients to describe in their own words their experiences of living with itch and how they were coping with it. This allowed an undirected approach to the investigation of this symptom whereby patients' personal accounts could be documented.

The total number of survey respondents and the number of respondents per question were counted. The percentage of patients who fell into each category (i.e. each question) was recorded.

## RESULTS

Not all the respondents addressed all the questions; therefore, the common denominator varied among the different topics addressed. A total of 238 subjects responded to the survey (231 women, 97%) (Table I). The age group of the study participants ranged from 20

Table I. *Characteristics of patients completing the internet survey*

| Variables | *n* (%) |
|---|---|
| Total respondents | 238 |
| Women | 231 (97) |
| Reported itch | 165 (69.3) |



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Table II. *Itch questionnaire*

| | | | |
|---|---|---|---|
| Do you have itch? (*n*=239) | | | |
| *Yes* | *No* | | |
| 165 (69%) | 74 (31%) | | |
| How long have you been itching? (*n* = 165) | | | |
| *0–5 years* | *6–10 years* | *>10 years* | |
| 88 (53%) | 42 (25%) | 35 (22%) | |
| Did you itch prior to your PBC diagnosis? (*n*=165) | | | |
| *Yes* | *No* | | |
| 124 (75%) | 41 (25%) | | |
| When and how did you learn that your itch was due to liver disease? (Left blank) | | | |
| In your own words describe the sensation of your itch. (see Table III) | | | |
| What makes the itch better? (*n*=88) | | | |
| *Something cool* | *Scratching* | *Nothing* | |
| 57 (65%) | 12 (14%) | 19 (22%) | |
| What makes the itch worse? (*n*=112) | | | |
| *Some form of heat* | *Wearing clothes* | *Eating food* | *Dry skin* |
| 69 (61.6%) | 23 (20.5%) | 16 (14.2%) | 4 (3.5%) |
| Is the itch worse after eating? (see former question) | | | |
| Is the itch worse during the day, night or is it the same? (*n*=164) | | | |
| *Day* | *Night* | *Same* | |
| 12 (7.3%) | 107 (65.2%) | 45 (27.4%) | |
| Do you itch more before your menstrual periods? (*n*=53) | | | |
| *Yes* | *No* | | |
| 13 (24.5%) | 40 (75.5%) | | |
| Does the itch interfere with your sleep? (*n*=162) | | | |
| *Yes* | *No* | | |
| 120 (74%) | 42 (26%) | | |
| During which season is your itch worse? (*n*=52) | | | |
| *Summer* | *Winter* | *Spring* | *Winter/Summer* |
| 24 (46%) | 20 (38%) | 2 (4%) | 1 (2%) |
| *Winter/Spring* | *Spring/Summer* | *Winter/Fall* | |
| 3 (6%) | 1 (2%) | 1 (2%) | |
| Were you prescribed any of the following for your itch, and if yes, did it help? *Nothing, cholestyramine, antihistamines, creams, rifampin, prednisone, antibiotics, naloxone, naltrexone, ondansetron, antidepressants, UV light, plasmaphresis. (see Table V)* | | | |
| What is the most effective treatment for your itch? (see Table VI) | | | |
| How does your doctor evaluate your itch? (see Table IV) | | | |

PBC: primary biliary cirrhosis.

to over 71 years with the majority in the 51–60 years age group (*n*=107). A total of 165 subjects reported that they had itch (69.3%). The questions included in the questionnaire on itch along with the responses are reported in table II. One hundred and twenty-four (75%) of those with itch reported that they itched prior to their diagnosis of PBC, most of them stating that they had been itching for 2–5 years before the diagnosis. Patients were asked to describe the sensation of their itch in their own words. A total of 164 patients reported descriptions on the sensation of itch; some patients used more than one qualifying statement to describe their itch (Table II). The most consistent responses were "bugs crawling" from 58 of 164 (35%) respondents, and "deep itch" from 48 (29.2%). Twenty-nine subjects (17.6%) stated that the itch was "relentless" or so severe that it led to wanting to "tear their skin off" and 6 responses (3.6 %) stated that the subjects scratched until they bled (Table III). When asked what made the itch better, 57 of 88 respondents (64.7%) reported "something cool" and 19 (21.5%) reported that nothing made their itch better. When asked what made the itch worse, 69 of 112 respondents (61.6%) reported heat, 23 (20.5%) reported "wearing clothes" and 4 (3.5%) reported, "dry skin".

A total of 120 of 162 respondents (74%) reported that their itch affected their sleep, 16 of 112 respondents (14.2%) reported worsening of itch after eating, and 107 of 164 respondents (65.2%) stated that their itch was worse at night. Of the 53 subjects that answered the questions on the effect of menstruation on itch, 13 (24.5%) reported an increase in their itch before menstruation. A total of 24 of 52 (46%) respondents reported that their itch was worse in the summer, and 20 (38%) in the winter. A total of 104 subjects of 149 (69.7%) reported that their doctor did not evaluate their itch (Table IV). Forty-seven of the 164 (28.6%) respondents who answered the question of how their itch was treated reported that they had not been given medications, 74 (45.1%) had been prescribed antihistamines, and 72 (43.9%) cholestyramine (Table V). Twenty-seven of 123 (21.9%) respondents reported that antihistamines had been the most effective treatment for their itch (Table VI), and 19 (14.3 %) reported that "nothing" had relieved their itch.

## DISCUSSION

The findings of this study suggest that itch in PBC adversely affects sleep, it is worse at night, and, in

Table III. *Description of itch (n=201)*

| "Bugs crawling" | "Deep relentless" | "Want to tear my skin off" | "Prickly/ needles" | "Bugs crawling + deep itch" | "Burning" | "Itch until I bleed" | "Hives" | "Urgent itch" |
|---|---|---|---|---|---|---|---|---|
| 58 (35%) | 48 (29.2%) | 29 (17.6%) | 25 (15.2%) | 16 (9.6%) | 13 (7.9%) | 6 (3.6%) | 5 (3%) | 1 (0.6%) |

Table IV. *How does your doctor evaluate your itch? (n=149)*

| Does not evaluate | Talks to me | Questionnaire | VAS | Questionnaire + VAS | Looks at my skin |
|---|---|---|---|---|---|
| 104 (69.8%) | 22 (14.8%) | 9 (6%) | 9 (6%) | 2 (1.3%) | 3 (2%) |

VAS: visual analogue scale,

Table V. *Number of patients prescribed medications and number of patients in whom the medications relieved their itch. Respondents: 164; patients had been prescribed more than one drug*

| Drug | Patients prescribed a drug *n* (%) | Patients helped by the drug *n* (%) |
|---|---|---|
| Nothing | 47 (28.6) | N/A |
| Antihistamines | 74 (45.1) | 47 (63.5) |
| Cholestyramine | 72 (43.9) | 39 (54.1) |
| Creams | 39 (23.7) | 23 (58.9) |
| Prednisone | 26 (15.8) | 23 (88.4) |
| Antidepressants | 21 (12.8) | 5 (23.8) |
| Rifampicin | 21 (12.8) | 12 (57) |
| Antibiotics* | 6 (3.6) | 1(16.6) |
| Naloxone | 6 (3.6) | 0 |
| Naltrexone | 2 (1.2) | 1 (50) |
| Ondansetron | 5 (3) | 2 (40) |
| Ultraviolet light | 1 (0.6) | 0 |
| Other | 6 (3.6) | 1 (16.6) |

*: antibiotics different from rifampicin
N/A: non-applicable

some patients, it can be worse after meals and pre-menstrually. The itch was described as a sensation of "bugs crawling" and a "deep itch", which, at times, was "relentless" and made those with this sensation want to tear their skin off or scratch until they bled. These descriptions suggest that the itch can be severe. It was reported that the itch was alleviated at times by applying something cool to the skin and exacerbated by heat and clothes in a substantial number of patients. This type of itch could precede the diagnosis of PBC by several years, which emphasizes the importance of considering PBC in the differential diagnosis of itch, when it is not associated with pruritic skin lesions.

In this survey the most common forms of treatment for itch were antihistamine drugs, reported to be helpful in 63.5% of respondents, and cholestyramine, helpful in 54.1%. Prednisone, which had been prescribed in 15.8% of the respondents, was helpful in 88.1%. Of these, antihistamines were reported as being helpful to those who took them for itch (64%), followed by prednisone (62%), creams (58%) and rifampin (57%). The study did not determine whether antihistamines decreased the sensation of itch, or whether they resulted in sedation, an expected side-effect of these drugs (13). Some patients reported that their itch was alleviated by creams; this may be due to the cooling and hydrating properties of these preparations. The rationale behind the use of prednisone cannot be inferred by this study. In fact prednisone may have a deleterious effect in patients with PBC as it may accelerate the rate of osteoporosis (14). It is possible that the mood-enhancing effect of steroids may have altered the perception of itch to some degree. Any effect that steroids may have on the metabolizing pathways in the liver that may affect the systemic availability of the pruritogens remains to be explored. The use of opiate antagonists to treat itch in PBC has a scientific rationale and has been shown to decrease itch in cholestasis in controlled studies that applied objective methodology (8, 15–17); however, only 7 out of 117 (6%) patients reported that they had received this type of drug.

Table VI. *The most effective treatment for itch (respondents: 123)*

| Treatment | Total *n* (%) |
|---|---|
| Antihistamines | 27 (21.9) |
| Cream | 16 (13) |
| Something cool | 15 (12.1) |
| Cholestyramine | 14 (11.3) |
| UDCA | 13 (10.5) |
| Scratching | 8 (6.5) |
| Rifampin | 7 (5.6) |
| Naltrexone | 2 (1.6) |
| Antidepressants | 2 (1.6) |

UDCA: ursodeoxycholic acid.

It can be concluded from the results of this study that there is no consistent mode of treatment for itch in PBC throughout the USA. There appears to be a lack of awareness of evolving concepts that have an impact on the treatment of itch in PBC (8, 15–17). According to the participants in this study, their physicians did not evaluate their itch even though the majority of the patients reported that the itch affected their sleep. These results underscore the tremendous need to educate patients and physicians caring for patients with this disease.

Consistent with our hypothesis, the results of this survey have provided some information on how patients experience itch, and how it can affect their lives negatively. There have been very few previous studies reporting the patients' characterization of their itch in their own words. Therefore, the results of the study provide a window into the lives of patients with PBC and chronic itch. Given the destructive nature of itch in PBC, this may provide impetus for research in this important clinical area.

Also consistent with our hypothesis is that the results of this survey may allow some inference on the pathophysiology of itch in PBC. For example, the fact that itch was reported to worsen in the pre-menstrual period by 24.5% of the subjects who reported on the effect of menstruation of their itch suggests that hormonal factors may influence the perception of itch, and the increase in pruritus caused by eating suggests that pruritogens or co-factors of pruritogens may be excreted in bile, which is poured into the duodenum after a meal. Analysis of these results, however, allows us to propose an additional consideration. The majority of patients did not report an increase in itch in the premenstrual period or after meals; this information may support the importance of the patients' genetic make-up in the perception of itch. In this context, a single nucleotide polymorphism in the gene that codes for MDR2, one of the transporters located on the cannalicular side of the hepatocyte, has

been identified in a group of patients with PBC and itch (18). These findings suggest that certain genetic characteristics predispose patients to, or protect them from, itch in cholestasis due to PBC. In fact, and consistent with a patient-dependent factor, some patients with profound cholestasis never report itch.

This study has several limitations. The survey addressed the use of prescribed medications or other interventions to treat itch in PBC, and not drugs that the patients might have been taking for other conditions; thus, whether any other drugs contributed to the itch reported by these patients is unknown. The fact that 69% of patients reported itching, however, tends to suggest that the itch was indeed due to PBC, as this percentage falls within the range of the prevalence of itch in patients with PBC reported in the literature (2). It is likely that most of the patients who responded to the survey had easy access to the internet, excluding patients who do not have that option; however, most of the communication among the patient members of the PBCers Organization is on-line. Therefore it is an inevitable limitation of the study. This may be an inevitable bias in the study as the questionnaire was internet based. In addition, perhaps it was mostly patients who experienced itch who were motivated to respond. The findings of the study, however, indicate that itch associated with PBC can seriously affect the lives of patients living with this disease.

Itch is one of the most common symptoms of PBC, and it can present years before the diagnosis of this liver disease is made; accordingly, this disease has to be included in the differential diagnosis of patients presenting with itch, without a primary rash, and with itch and abnormal hepatic panel, regardless of the presence of itch. As dermatologists tend to be the first specialists to evaluate patients with itch, dissemination of information on PBC to these specialists seems to be highly relevant to good practice in clinical medicine. Given the limited options for treating itch in PBC, further research into the etiology of this symptom is needed.

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