

Collecting clinical data during an emergency: quality of life in primary biliary cholangitis during the COVID-19 pandemic

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ABSTRACT

Background. Primary biliary cholangitis (PBC) is a chronic autoimmune liver disease. As an infrequent disease, a Facebook group was created for patients to share experiences and problems. In fact, during the COVID-19 pandemic, patient analysis could only be done through remote connection systems. Therefore, to analyze patients' quality of life (QoL), we exploited social networks and online data collection platforms. **Objectives.** A survey was carried out to evaluate the QoL of patients with PBC

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during the COVID-19 pandemic. **Materials and Methods.** A Facebook group was used for patient enrolment. Age, sex, diagnosis, years since diagnosis, associated diseases, histological stage of the disease, value of elastography, and current therapy were collected. PBC 40 online questionnaire was submitted to patients to assess their QoL. **Results.** 78 patients participated in the study: 75 females, and 3 males, the mean (\pm SD) age was 46.4 \pm 11.5. The main diagnoses were PBC in 66 patients and overlapping syndrome PBC + autoimmune hepatitis in 10. Histology was available in 45 patients, of whom 34 were stages 1-2 and 11 stages 3-4. The main therapy was ursodeoxycholic acid in 56 pts. The questionnaire is divided into 6 domains, covering fatigue, emotional, social, and cognitive functions, general symptoms, and itching. The mean and standard deviation of the scores were computed. Interpretation of the results obtained by applying a quantitative scale showed no impairment for social, mild impairment for general symptoms, itching, cognitive and emotional function, and moderate impairment for fatigue. No correlation was found between scores and disease duration. **Conclusions.** This study demonstrates that online questionnaires are a viable substitute for paper questionnaires and that data collected from online surveys on Facebook can have scientific relevance; PBC had the greatest impact on QoL on fatigue and the least on social aspects.

Introduction

During the pandemic, some flaws in the healthcare system emerged. In particular, the difficulty of moving patients to general practitioners and outpatient clinics or general and university hospitals made constant monitoring of the disease complex. Patients with rare diseases, who require regular check-ups have encountered great difficulties. One possibility to solve this problem is using social networks. As well known, the use of the Internet, the availability of low-cost connected devices (e.g., smartphones or tablets), and the spreading of social networks have exponentially increased human remote interaction capabilities. Nowadays there are many

examples of the use of surveys done on the Internet for market analysis or to collect subjective judgments. With this paper, we want to show that an online survey, using popular social networks, can be used in circumstances where it is not possible to easily reach the patient.

In recent years, we have witnessed the proliferation of spontaneous patient groups created to share information, concerns, diagnosis, treatment, and comments about their disease.

Primary biliary cholangitis (PBC) is an infrequent immune-mediated cholestatic liver disease characterized by progressive inflammation of the interlobular bile ducts. In Italy, the estimated incidence and prevalence of the disease are, respectively, 2.21-5.31 and 3.86-27.9 per 100,000 inhabitants.¹ If not properly treated, the disease can progress to liver failure requiring transplantation; therefore, early diagnosis and proper staging of the disease are essential.

Popular social networks, such as Facebook, have been used as a sharing platform. In particular, a private Facebook group named “Primary Biliary Cholangitis and Chronic Autoimmune Hepatitis” with 819 members was founded on June 5th, 2015. Of these, 78 agreed to participate and filled out the questionnaires during the period of national health emergency (9 March - 18 May 2020).

Materials and Methods

The group administrator was contacted and informed about the purpose of the study and agreed to join the project. The Facebook group involved in the study had 819 members affected by PBC or chronic autoimmune hepatitis (AIH), and only patients with PBC or overlapping syndrome (OS) were enrolled. The exact number of PBC members in the Facebook group is not known to us, since participation in the questionnaire was on a voluntary basis.

The PBC 40 model, widely validated and translated into several languages, was used as a tool for assessing the quality of life (QoL) of patients with PBC.² A Google Form with the Italian translation of the questionnaire was made adding information on the use and storage of personal data. The survey was totally anonymous,

according to the “Regulation 2016/679” of the European Parliament and the Council of April 27th, 2016, as well as Legislative Decree 196/03.

Age, sex, diagnosis, years from diagnosis, associated diseases, histological stage of the disease, value of elastography as assessed by Fibroscan, and therapies taken were requested. The 40 questions of the PBC 40 questionnaire were grouped into six domains: general symptoms, itch, fatigue, cognitive, social, and emotional functions. Each question was assigned a score from 1 to 5, where 1 corresponded to minimum impact and 5 to maximum impact. The score for each domain was calculated by summing individual question response scores, and, to clinically define symptom severity, the score ranges were assessed according to Newton JL *et al.*, as shown in Table 1.³

Statistical analysis

Continuous data were summarized with mean, standard deviation, range, and median; categorical data were summarized with counts and percentages.

Cronbach's alpha, which is a measure of internal consistency (*i.e.*, how closely a set of items is related as a group), was performed. We also performed error bars indicating the uncertainty of the estimate (95% confidence interval). All statistical analyses presented in this article are only descriptive. STATA v.16 was used to perform them.

Results and Discussion

Demographic and clinical characteristics of sample

78 patients agreed to participate in the survey and complete the questionnaire: 75 females, and 3 males, mean (\pm SD) age was 46.4 \pm 11.5, diagnosis was PBC in 66, overlapping syndrome PBC+AIH in 10, OS PBC + primary sclerosing cholangitis (PSC) in 1 and OS PBC+AIH+PSC in 1. The main associated diseases were: Sjogren in 15, autoimmune thyroiditis in 14, rheumatoid arthritis in 8, diabetes in 7, systemic sclerosis in 3, celiac disease in 2, Crohn in 1, and ulcerative colitis in 1; 28 patients reported other diseases.

The mean time between symptoms and diagnosis

Table 1. Defined score ranges for the primary biliary cholangitis-40 domain.

PBC-40 domain	None	Mild	Moderate	Severe
Symptoms	<7	8-18	19-25	>26
Itch	<3	4-8	9-11	>12
Fatigue	<11	12-28	29-39	>40
Cognitive	<6	7-15	16-21	>22
Social and emotional	<13	14-34	35-49	>50

PBC, primary biliary cholangitis.

was 4.3 years (median 3.0, range 0-20). Histology was available in 45 patients, of whom 34 were in stages 1-2 and 11 were in stages 3-4 (see Table 2).

Of the 33 patients without histology, 22 had performed at least an elastography for the staging of the disease, while 11 had not even performed it. 32 patients had undergone both elastography and biopsy. Among the 54 patients who had elastography, 36 had a liver stiffness between 0 and 7.3 kPa (F1), 7 between 7.4 and 9.8 kPa (F2), 6 between 9.9 and 17.3 kPa (F3) and 5 greater than 17.3 kPa (F4) (according to Corpechot) as shown in Table 3.⁴

Therapy was ursodeoxycholic acid (UDCA) in 56 pts, UDCA + obeticholic acid in 6 pts, UDCA + steroids in 8 pts, UDCA + fibrates in 4 pts, and other therapies in 4 pts.

PBC-40 questionnaire analysis

By grouping the 40 questions of the questionnaire into 6 groups (symptoms, itching, fatigue, cognition, social, and emotional), the values of the scores obtained by applying a quantitative scale are shown in Table 4.

The frequency of the patients by severity scores calculated by applying a previously published scale is summarized in Figure 1.³

As shown in Figure 1, mild and moderate severity scores are prevalent for the "Symptoms" item; for "Itch" no or mild severity scores are prevalent. For "Fatigue" mild, moderate, and severe scores are equally represented; for "Cognition" all severity scores are represented, mainly mild and moderate. "Emotional" shows no impact on the disease, while in "Social", mild severity scores are prevalent.

The greatest impact of the disease seems to be, in our sample, on fatigue and cognition, followed by symptoms, while the least impact was on emotional function.

Table 2. Patients' characteristics.

Patients, n	78
Age [years] (mean±SD)	46.4±11.5
Male, n (%)	3 (3.8)
Female, n (%)	75 (96.2)
Diagnosis, n	
PBC	66
PBC+AIH	10
PBC+PSC	1
PBC+AIH+PSC	1
Time to diagnosis [years] (mean±SD)	4.3±4.5
Associated Diseases, n	
Sjogren	15
Autoimmune thyroiditis	14
Rheumatoid arthritis	8
Diabetes	7
Systemic sclerosis	3
Celiac disease	2
IBD	2
Other diseases	28
Histological stage (n=45)	
1-2	34
3-4	11

PBC, primary biliary cholangitis; AIH, autoimmune hepatitis; PSC, primary sclerosing cholangitis; IBD, inflammatory bowel disease.

Table 3. Stage of disease according to liver stiffness value (n=54).

Liver Stiffness [kPa]	Stage	N
0-7.3	F1	36
7.4-9.8	F2	7
9.9-17.3	F3	6
>17.3	F4	5

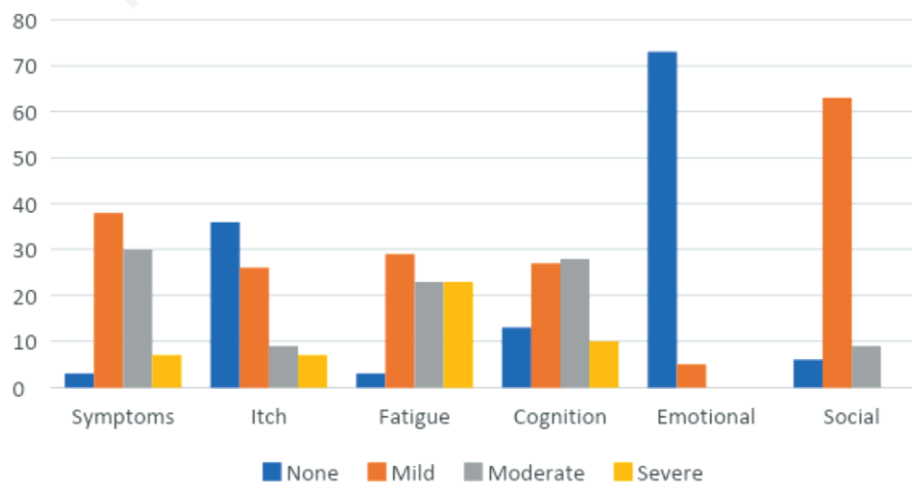


Figure 1. Distribution of patients by severity scores, for six domains.

The percentage distribution of the patients by years from diagnosis: 30% of the sample had a diagnosis 1 year before, 47% from 2 to 5 years before, and 23% more than 6 years before.

Patient distribution in each domain was analyzed by

severity scores and disease duration and was divided into 3 periods: ≤ 1 year, 2 to 5 years, and 6 to more years; however, no statistically significant differences were found (Figure 2).

Analysis of data using error bar plots (not shown in

Table 4. Score of the six domains.

	Symptoms	Itch	Fatigue	Cognition	Social	Emotional
Mean	18.26	5.55	30.62	14.65	8.38	24.27
SD	5.80	3.34	11.98	6.11	2.95	7.50
Minimum	7.00	3.00	11.00	6.00	3.00	10.00
Maximum	31.00	15.00	53.00	30.00	15.00	41.00
Median	18.00	4.00	32.00	15.00	8.00	24.00

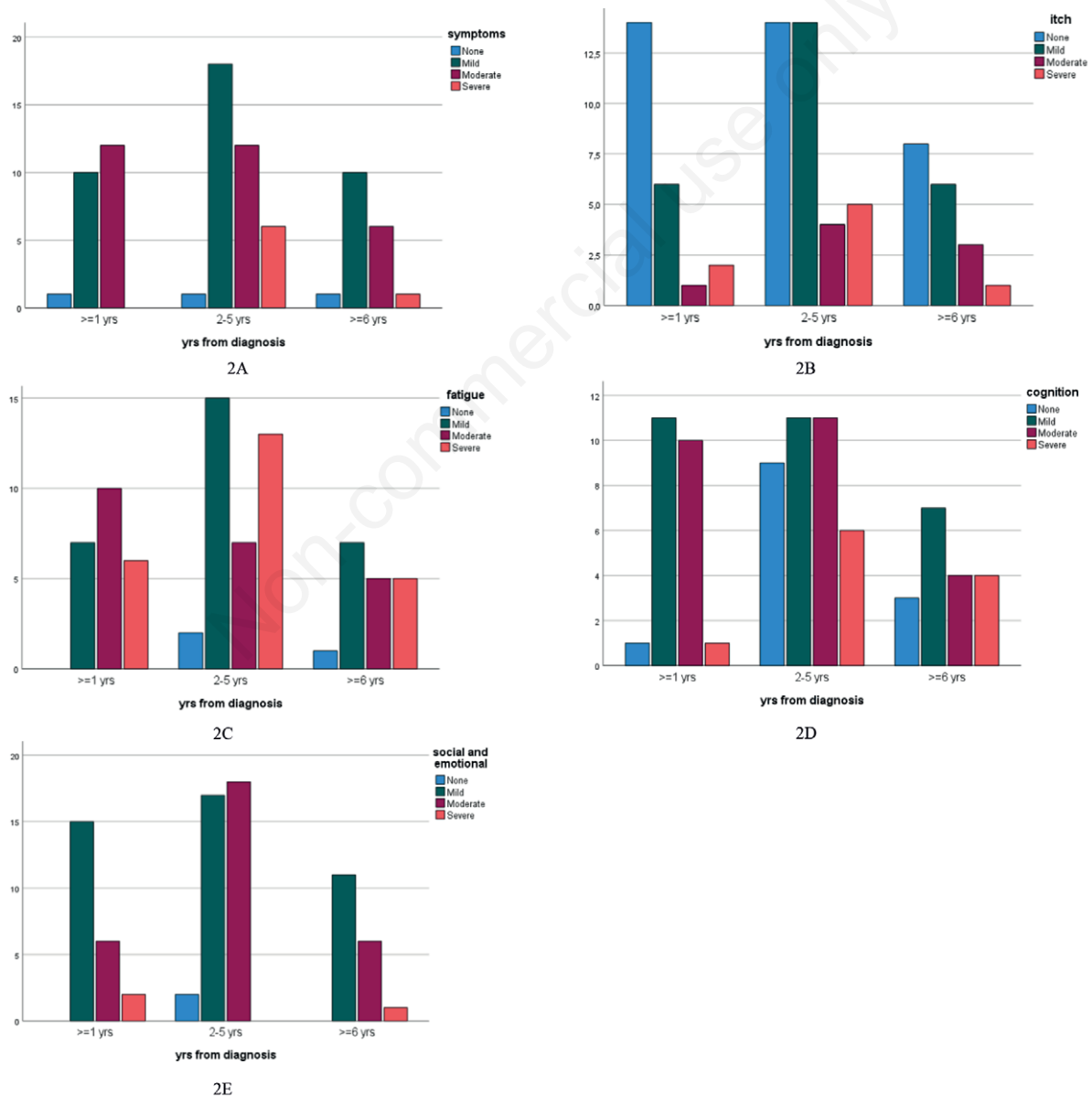


Figure 2. Distribution of patients by severity score and years from diagnosis.

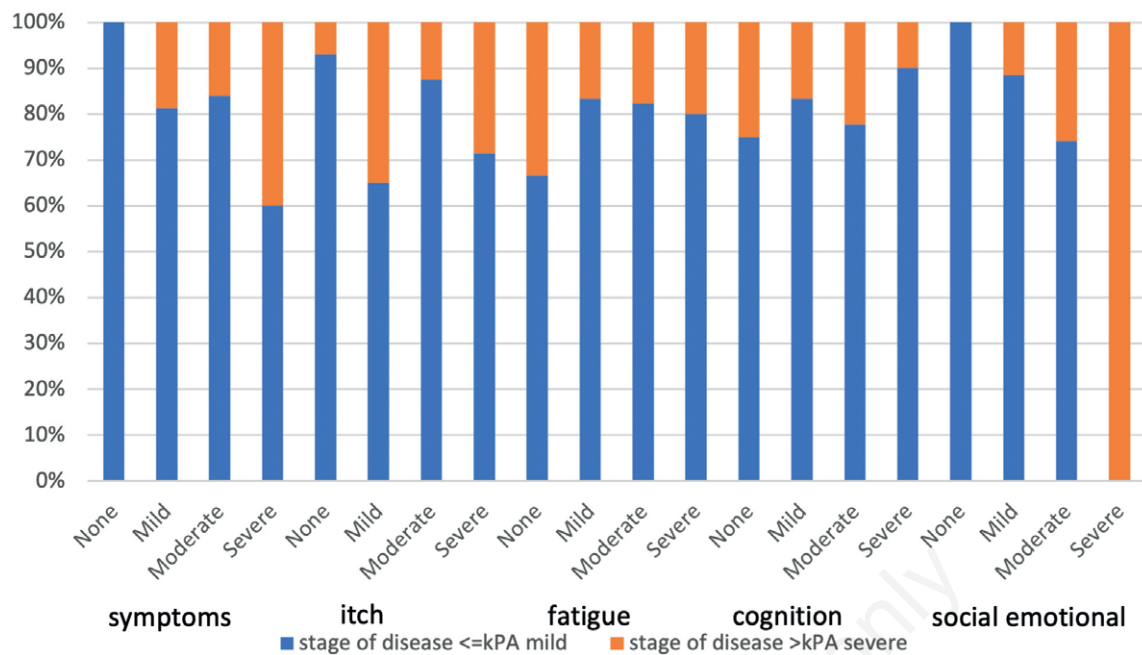


Figure 3. Distribution of patients by severity scores and stage of disease, for six domains.

this paper) for severity scores and years since diagnosis reveals wide variability. Nevertheless, for the item “itch” there is a trend of increasing severity in relation to the years since diagnosis (a higher value of moderate itch is shown 2-5 years after diagnosis then decreases; the confidence intervals are very wide due to the small sample size); “fatigue” seems quite stable over the years, while “cognition” shows an increasing trend in severity related to years since diagnosis. “Social” and “emotional” appear stable over time.

The distribution of patients in each domain was also analyzed according to the severity scores and the stage of the disease (histological or derived from elastography), but no statistically significant differences were found (Figure 3).

Cronbach’s alpha is very high (equal to 0,956, also standardized), suggesting that the items have relatively high internal consistency.

The main criticisms of this study could be the following: i) the methods used for data collection are remote qualitative. We used self-completed online questionnaires, shared via social media platforms, which became essential during the COVID-19 era.⁵ In addition, for this qualitative research, a convenience sample has been recruited through online social networking platforms. Therefore, the sample is not representative of the target population of Italian people affected by PBC because in this study there is no reliable sampling frame for online surveys, and participants were not selected by a randomized or probability sampling method; ii) furthermore, response rates (*i.e.*, how many of the total number of people who viewed the sur-

vey link responded) are not available.⁶ For these reasons, the results obtained are not comparable with those of cohort studies of patients assisted by general practitioners;⁷ iii) another possible bias introduced in the results could derive from the online survey administration mode, which is often described as “the measurement effect”.⁸ This could be due to differences in the participants’ level of engagement, understanding of the questions, and social desirability bias experienced in different survey administration methods (*i.e.*, traditional paper-based *vs.* online survey).

Despite all the limitations mentioned, the results allow us to claim that in cases where direct contact with patients is not feasible, it is still possible to administer psychological questionnaires through social media. Analysis and processing of the results can be performed in a very short time, being able to discuss with patients in chat rooms or webinars, achieving positive effects on their psychological conditions, and positively influencing their attitude toward the disease.

Conclusions

In this contribution we have shown that: i) patients are eager to contribute to the study by answering the questionnaire and also to feel useful and part of a group; ii) online questionnaires are a valid substitute for paper questionnaires; iii) data collected from online surveys on Facebook are qualitative they are affected by selection bias, thus cannot be representative of a target population. Furthermore, data collected through online

surveys may suffer from the intrinsic limitation of being based on the possibility of the user having Internet access.

Nevertheless, in this small convenience sample of Italian PBC patients, it seems that the greater impact of the disease on QoL was on fatigue and the least on social items.

This is an example of how data can be collected through online surveys. Surely, it suffers from the intrinsic limitation of being based on the possibility of the user having Internet access. Our hypothesis is that the Internet will spread all over the country.

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