

Original Study Article

DOI: <https://doi.org/10.17816/uds682920>

EDN: YYZVHO

Impact of Primary Biliary Cholangitis Severity on Oral Health Status

Anna R. Khokhlova¹, Natalia S. Robakidze¹, Karina L. Raykhelson², Margarita V. Klur¹¹ North-Western State Medical University named after I.I. Mechnikov, Saint Petersburg, Russia;² Saint Petersburg State University, Saint Petersburg, Russia

ABSTRACT

BACKGROUND: Primary biliary cholangitis (PBC) is a chronic immune-mediated liver disease predominantly affecting women (prevalence: 2–40 cases per 100,000 population). It is often accompanied by xerostomia and marked oral changes. The pathogenetic mechanisms linking oral pathology and autoimmune liver disease remain poorly investigated.

AIM: This work aimed to correlate the pattern of oral changes in patients with PBC with disease duration, stage, and clinical-course characteristics.

METHODS: Forty-eight women aged 43 to 69 years with confirmed PBC were examined. Disease stage (early or advanced) was determined using laboratory data and transient elastography. Oral assessment included clinical dental examination, radiography, evaluation of salivary gland function (sialometry, salivary pH measurement, ultrasonography), and detection of key periodontopathogens via polymerase chain reaction. Statistical analysis was conducted using R software with regression modeling.

RESULTS: Advanced-stage PBC was identified in 52% of cases; xerostomia was present in 68.75%. Liver stiffness was positively correlated with xerostomia severity ($\tau = 0.54$, $p < 0.001$), periodontitis stage ($\tau = 0.56$, $p < 0.001$), and oral-hygiene status as well as the number of identified periodontopathogens. More severe oral abnormalities were observed with longer disease duration. Gamma-glutamyltransferase and alanine aminotransferase levels showed positive correlations with xerostomia and periodontitis severity.

CONCLUSION: Oral abnormalities in patients with PBC are closely associated with disease severity, duration, and liver function biomarkers. These changes may serve as supplementary clinical indicators of disease progression and support the need for a multidisciplinary approach to management.

Keywords: primary biliary cholangitis; xerostomia; oral-hygiene status.

To cite this article

Khokhlova AR, Robakidze NS, Raykhelson KL, Klur MV. Impact of Primary Biliary Cholangitis Severity on Oral Health Status. *Acta Universitatis Dentistriae et Chirurgiae Maxillofacialis*. 2025;3(2):67–72. DOI: 10.17816/uds682920 EDN: YYZVHO

Submitted: 04.06.2025

Accepted: 17.06.2025

Published online: 31.07.2025

Оригинальное исследование

DOI: <https://doi.org/10.17816/uds682920>

EDN: YYZVHO

Влияние тяжести течения первичного билиарного холангита на состояние полости рта

А.Р. Хохлова¹, Н.С. Робакидзе¹, К.Л. Райхельсон², М.В. Клур¹¹ Северо-Западный государственный медицинский университет им. И.И. Мечникова, Санкт-Петербург, Россия;² Санкт-Петербургский государственный университет, Санкт-Петербург, Россия

АННОТАЦИЯ

Обоснование. Первичный билиарный холангит — хроническое иммуно-опосредованное заболевание печени, наблюдающееся преимущественно у женщин (распространенность 2–40 случаев на 100 тыс. населения), которое сопровождается развитием ксеростомии и выраженных изменений полости рта. Патогенетические аспекты взаимосвязи стоматологической патологии и аутоиммунного заболевания печени мало изучены.

Цель — сопоставить характер изменений в полости рта при первичном билиарном холангите с длительностью, стадией и особенностями течения заболевания печени.

Методы. Обследовано 48 женщин с подтвержденным диагнозом первичного билиарного холангита в возрасте от 43 до 69 лет. Стадию заболевания (ранняя, поздняя) устанавливали на основании лабораторных данных и результатов транзитной эластометрии печени. Анализ состояния полости рта включал клинический стоматологический осмотр, рентгенологическое исследование, оценку функции слюнных желез (сиалометрия, измерение pH слюнных желез, ультразвуковое исследование слюнных желез), диагностику основных пародонтопатогенов методом полимеразной цепной реакции. Статистический анализ проводился в программной среде «R» с применением моделей регрессии.

Результаты. В 52% наблюдений установлена поздняя стадия первичного билиарного холангита, у 68,75% больных отмечена ксеростомия. Установлена прямая корреляция между жесткостью печени и степенью ксеростомии ($\tau=0,54$, $p<0,001$), стадией пародонтита ($\tau=0,56$, $p<0,001$), а также гигиеническим состоянием рта и количеством выявленных пародонтопатогенов. Более тяжелые стоматологические нарушения регистрировались при большей давности заболевания. Уровни гамма-глутамилтрансферазы и аланинаминотрансферазы положительно коррелировали с показателями ксеростомии и тяжестью пародонтита.

Заключение. Нарушения в полости рта при первичном билиарном холангите тесно связаны с тяжестью и длительностью основного заболевания, а также с лабораторными показателями функции печени. Эти изменения могут использоваться как дополнительные клинические маркеры, отражающие прогрессирование первичного билиарного холангита и необходимость комплексного междисциплинарного подхода к лечению.

Ключевые слова: первичный билиарный холангит; ксеростомия; гигиеническое состояние ротовой полости.

Как цитировать

Хохлова А.Р., Робакидзе Н.С., Райхельсон К.Л., Клур М.В. Влияние тяжести течения первичного билиарного холангита на состояние полости рта // Университетская стоматология и челюстно-лицевая хирургия. 2025. Т. 3, № 2. С. 67–72. DOI: 10.17816/uds682920 EDN: YYZVHO

BACKGROUND

Primary biliary cholangitis (PBC) is a granulomatous, non-suppurative, destructive cholangitis that develops as a result of immune-mediated injury to the biliary epithelium of small intrahepatic bile ducts, leading to cholestasis and progressive fibrosis up to the terminal stage of biliary cirrhosis. Although PBC is considered a relatively rare disease, it nevertheless poses a significant public health challenge [1]. According to various studies, the global incidence of PBC is steadily increasing, with prevalence ranging from 1.9 to 58 cases per 100,000 population [2–4].

PBC is diagnosed predominantly in women, accounting for up to 95% of cases, most commonly between the ages of 50 and 65 years. Given global demographic trends characterized by population aging and the rising prevalence of autoimmune disorders in recent decades, there is a reasonable assumption that the frequency of PBC detection will continue to increase [5–7].

Since PBC, as well as the associated Sjögren syndrome (SS) [8–10], is accompanied by xerostomia [11], pathological changes develop in the oral cavity, leading to deterioration of oral hygiene, increased caries activity [12–13], and alterations in the oral microbiota [14–15]. Such disturbances promote the formation of chronic inflammatory foci [16], which act as factors in the progression and maintenance of the autoimmune process occurring in liver tissue, thereby negatively affecting the general condition of patients and contributing to an unfavorable disease prognosis [17].

The aim of the study was to compare the characteristics of oral cavity changes in patients with PBC with the duration, stage, and clinical features of liver disease.

METHODS

A total of 48 female patients aged 43–69 years with a confirmed diagnosis of PBC, residing in St. Petersburg and the Leningrad region, and receiving outpatient treatment, were examined.

The diagnosis of PBC was established based on the presence of at least two of the three criteria recommended by the European Association for the Study of the Liver (EASL) and the American Association for the Study of Liver Diseases: elevated serum alkaline phosphatase, the presence of pathognomonic autoantibodies (antimitochondrial antibodies, antinuclear antibodies with indirect immunofluorescence patterns AC-6 and AC-12, anti-gp210, anti-sp-100), and histopathological findings [18]. All patients underwent medical history collection, physical examination, and laboratory testing, including clinical and biochemical blood analysis with the assessment of alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP),

gamma-glutamyltransferase (GGT), albumin, bilirubin, and international normalized ratio. Liver stiffness was measured using transient elastography (FibroScan®, Echosens, France). Disease stage (early or late) was determined according to the EASL (2017) criteria, based on laboratory results and transient elastography with a threshold value of 9.6 kPa. To assess SS, the Schirmer test (tear fluid production) and sialometry according to the method of Pozharnitskaya (detection and grading of xerostomia) were performed [19].

The assessment of oral cavity status was based on clinical guidelines [20]. The following indices were assessed: the Greene–Vermillion hygiene index (OHI-S), the decayed, missing, and filled teeth index (DMFT), the papillary-marginal-alveolar index (PMA), and the sulcus bleeding index (SBI). Periodontal status was evaluated by assessing tooth mobility, probing pocket depth, and radiographic findings.

To detect DNA of major periodontopathogenic microorganisms, the Dentoscreen test system (Litekh, Russia) based on the polymerase chain reaction (PCR) was used.

Data cleaning, structuring, and analysis were carried out using the R environment (version 4.4.2). For nominal variables, mode or median values were calculated as measures of central tendency; for ratio-scale or absolute variables, the median, first quartile (*LQ*), third quartile (*HQ*), and median absolute deviation (*MAD*) were determined. Associations between clinical and laboratory parameters, the DMFT index, stage of periodontitis, and degree of xerostomia were analyzed taking into account the simultaneous influence of several factors, using a cumulative link model for ordinal regression (clm algorithm from the ordinal package), multiple regression (glm algorithm with Gaussian distribution), and Poisson multiple regression. The critical level of statistical significance for the null hypothesis was set at 0.05.

RESULTS

The duration of PBC from the onset of first clinical manifestations ranged from 4 to 18 years, with a mean of 10.1 ± 3.5 years, whereas the duration from the time of diagnosis ranged from 1 to 15 years, with a mean of 7.6 ± 3.2 years. The late stage of the disease was identified in 25 patients (52.1%), of whom 8 (16.7%) were diagnosed with liver cirrhosis.

The main complaints were as follows: weakness in 41 patients (85.0%), sleep disturbances in 38 (79.0%), pruritus of varying severity in 20 (42.0%), jaundice in 5 (10.4%), and heaviness in the right hypochondrium in 8 (16.7%). Complaints of oral dryness were reported by 68.75% of patients ($n = 33$). Persistent xerostomia was noted in 54.17% of patients ($n = 26$), while episodic xerostomia was noted in 14.58% of patients ($n = 7$). Difficulties with mastication, gingival bleeding and halitosis

Table 1. Association between xerostomia severity and duration of liver disease

Таблица 1. Зависимость тяжести ксеростомии от длительности заболевания печени

Duration of primary biliary cholangitis	No xerostomia	Early stage	Pronounced stage	Late stage	Kendall τ	p
Up to 6 years ($n = 5$)	2 (4.2%)	2 (4.2%)	1 (2.1%)	0 (0%)	0.51	<0.001
6–12 years ($n = 30$)	7 (14.6%)	2 (4.2%)	17 (35.4%)	4 (8.3%)		
More than 12 years ($n = 13$)	0 (0%)	1 (2.1%)	6 (12.5%)	6 (12.5%)		
Total ($n = 48$)	9	5	24	10		

were observed in 47.92% ($n = 23$), 60.42% ($n = 29$), and 45.83% ($n = 22$) of patients, respectively. Nine patients with PBC (18.75%) had no signs of xerostomia; early-stage, advanced-stage and late-stage xerostomia was diagnosed in 5 patients (10.42%), 24 patients (50.00%), and 10 patients (20.83%), respectively. Oral hygiene quality was rated as good, satisfactory, unsatisfactory, and poor in 28.3% ($n = 13$), 39.1% ($n = 18$), 19.6% ($n = 9$), and 13.0% ($n = 6$) of cases, respectively.

Radiological signs of periodontal disease (destruction of cortical plates and resorption of interdental septa) were observed in all patients with PBC. The distribution of periodontal pocket depth was as follows: 1–2 mm in 15.56% of cases; 3 mm in 53.33% of cases; 4–5 mm in 17.78% of cases; and 6 mm in 13.33% of cases. A PMA index was <30% in 35.56% of patients ($n = 16$), 31%–60% in 46.67% of patients ($n = 21$), and >60% in 17.78% of patients ($n = 8$). The Mühlemann–Cowell index ranged from 1.1 to 2.0 in 46.67% of patients ($n = 21$) and from 2.1 to 3.0 in 15.56% of patients ($n = 7$). The distribution of periodontitis stages was as follows: mild in 26.67% of patients ($n = 12$), moderate in 44.44% of patients ($n = 20$), and severe in 28.89% of patients ($n = 13$).

PCR testing identified DNA fragments of all major periodontopathogens: *Porphyromonas gingivalis*, *Prevotella intermedia*, *Treponema denticola*, *Aggregatibacter actinomycetemcomitans*, *Tannerella forsythia*, *Fusobacterium nucleatum*, and *Porphyromonas endodontalis*. The mean number of periodontopathogens per patient increased with advancing stage of xerostomia: 1.4 microorganisms per person at stage 0, 4.2 at stage I, 4.1 at stage II, and 5.5 at stage III.

It was established that the severity of xerostomia increased with the duration of liver disease (see Table 1).

Disease duration was directly associated with liver stiffness, levels of cholestasis markers (GGT, ALP, bilirubin), and the presence of specific autoantibodies (AMA, ANA).

Comparative analysis of laboratory and instrumental data revealed a pronounced positive correlation between disease stage (liver stiffness by elastography) and the severity of xerostomia ($\tau = 0.54$, $p < 0.001$), as well as with periodontitis stage ($\tau = 0.56$, $p < 0.001$).

In addition, a moderate positive correlation was observed between liver stiffness and the presence of SS ($\tau = 0.42$, $p < 0.001$), oral hygiene status ($\tau = 0.49$, $p < 0.001$), and the number of detected periodontopathogens ($\tau = 0.34$, $p = 0.002$).

Positive correlations were also identified between GGT activity and the severity of xerostomia ($\tau = 0.45$, $p < .001$), oral hygiene status ($\tau = 0.49$, $p < 0.001$), and periodontitis stage ($\tau = 0.41$, $p < 0.001$). Significant associations were found between ALT levels and oral hygiene status ($\tau = 0.40$, $p < 0.001$), as well as periodontitis stage ($\tau = 0.41$, $p < 0.001$).

CONCLUSION

The study demonstrated a direct correlation between the number of years since the onset of PBC, liver disease stage, and xerostomia stage, as well as with the increasing severity of periodontitis and worsening oral hygiene indices. The findings indicate that oral health status reflects the progression of PBC and provides an additional source of clinical information. This underscores the need for regular dental follow-up in patients with PBC and the integration of dentists into the interdisciplinary care team for such patients.

ADDITIONAL INFO

Author contributions: A.R. Khokhlova: data curation, formal analysis, writing—original draft; N.S. Robakidze, K.L. Raykhelson, M.V. Klur: writing—review & editing. All the authors made a significant contribution to the development of the concept, research and preparation of the article, read and approved the final version before publication.

Ethics approval: The study was approved by the local ethics committee of the North-Western State University named after I.I. Mechnikov (protocol No. 4 dated 02.04.2025). All study participants signed an informed consent form before being included in the study. The study protocol was published in the journal “University Dentistry and Oral Surgery,” and the manuscript was submitted for review on 04.06.2025.

Consent for publication: The authors have obtained written informed voluntary consent from the patients to the processing and publication of personal data in a scientific journal, including its electronic version. The amount of data to be published has been agreed upon with the patients.

Funding source: The authors claim that there is no external funding when writing the article.

Disclosure of interests: The authors have no relationships, activities or interests for the last three years related with for-profit or not-for-profit third parties whose interests may be affected by the content of the article.

Statement of originality: When creating this work, the authors did not use previously published information (text, illustrations, or data).

Data availability statement: All data obtained in this study is available in the published article.

Generative AI: Generative AI technologies were not used for this article creation.

Acknowledgments: The authors express their gratitude to the staff of the Clinical Infectious Diseases Hospital named after S.P. Botkin (Russia, St. Petersburg), as well as to D.A. Gusev personally, for providing access to the patient's examination.

Provenance and peer-review: This work was submitted to the journal on an initiative basis and was reviewed according to the usual procedure. Two external reviewers and the scientific editor of the publication participated in the review process.

ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

Вклад авторов. А.Р. Хохлова — сбор и обработка материалов исследования, анализ полученных данных, написание текста; Н.С. Робакидзе — внесение окончательной правки; К.Л. Рахильсон — внесение окончательной правки; М.В. Клур — внесение окончательной правки. Все авторы внесли существенный вклад в разработку концепции, проведение исследования и подготовку статьи, прочли и одобрили финальную версию перед публикацией.

Этическая экспертиза. Проведение исследования одобрено локальным этическим комитетом Северо-Западного Государственного Университета им. И.И. Мечникова (протокол № 4 от 02.04.2025).

REFERENCES

1. Xu H, Yanny B. Primary biliary cholangitis: a review. *Gene Expression*. 2022;21(2):45–50. doi: 10.14218/GEJLR.2022.00013
2. Bakulin IG, Skazykayeva EV, Skalinskaya MI. Primary biliary cholangitis: modern concepts of diagnosis and treatment. *Opinion Leader*. 2020;(9): 48–54. EDN: NZTSXP (In Russ.)
3. Tanaka A, Mori M, Matsumoto K, et al. Increase trend in the prevalence and male-to-female ratio of primary biliary cholangitis, autoimmune hepatitis, and primary sclerosing cholangitis in Japan. *Hepatol Res*. 2019;49(8):881–889. doi: 10.1111/hepr.13342
4. Jeong SH. Current epidemiology and clinical characteristics of autoimmune liver diseases in South Korea. *Clin Mol Hepatol*. 2018;24(1):10–19. doi: 10.3350/cmh.2017.0066
5. Ilinsky IM, Tsurulnikova OM. Primary biliary cholangitis. *Russian Journal of Transplantology and Artificial Organs*. 2021;23(1):162–170. doi: 10.15825/1995-1191-2021-1-162-170 EDN: LSUGLM
6. Elovikova TM, Sablina SN, Grigoriev SS, et al. Sjogren's syndrome and osteoporosis in practice of a dental practitioner: clinical case study. *Actual Problems in Dentistry*. 2022;18(4):17–23. doi: 10.18481/2077-7566-2022-18-4-17-23 EDN: OOWARV
7. Wibawa IDN, Shalim CP. Geographical disparity in primary biliary cholangitis prevalence: a mini-review. *Gene Expression*. 2022;21(2):41–44. doi: 10.14218/GE.2022.00005
8. Bordan O, Norheim KB, Rødahl E, et al. Primary Sjogren's syndrome and the eye. *Surv Ophthalmol*. 2020;65(2):119–132. doi: 10.1016/j.survophthal.2019.10.004 EDN: GFSJCT
9. Federal clinical guidelines for rheumatology 2018. Russian Academy of Medical Sciences, Institute of Rheumatology, Moscow, Russia. Methods used for collecting/selecting evidence: search in electronic databases. Available from: <https://rheumatolog.ru/experts/klinicheskie-rekomendacii> Accessed: 29.04.2022. (In Russ.)
10. Belugina TN, Gracheva YN, Kuryaeva AM, et al. Sjogren syndrome in the therapeutic practice (clinical case). *University Proceedings. Volga Region. Medical Sciences*. 2022;3(63):5–14. doi: 10.21685/2072-3032-2022-3-1 EDN: LUYELU
11. Assy Z, Brand HS. A systematic review of the effects of acupuncture on xerostomia and hyposalivation. *BMC Complement Altern Med*. 2018;18(1):57. doi: 10.1186/s12906-018-2124-x EDN: ZHDBQS
12. Robakidze NS, Raykhelson KL, Khokhlova AR, Klur MV. A modern view on the relationship between the state of the oral cavity and autoimmune liver diseases. *The Dental Institute*. 2022;(4):98–99. EDN: BIGPXS

13. Balyan LN. *Clinical and experimental rationale for the choice of oral hygiene means and methods for patients with xerostomia*. [Dissertation abstract]. Yekaterinburg: Ural State Medical Academy; 2022. 16 p. (In Russ.)
14. Chirkova KE, Leshcheva EA, Orekhova LY, et al. The problem of xerostomia in modern dentistry and features of its clinical manifestations. *System Analysis and Management in Biomedical Systems*. 2024;23(2):83–89. doi: 10.36622/1682-6523.2024.23.2.012 EDN: GZHIZK
15. Gerasimova LP, Usmanova IN, Al-Kofish MA, et al. Analysis of the microbial composition of oral biotopes in young people depending on dental status. *Periodontology*. 2017;22(3):73–78. EDN: ZHVEWP
16. Khodzhaeva MY, Yakubova LK, Mukhamedov I. Evaluation of biochemical factors leading to xerostomia. *Internauka*. 2021;(8–1):43–47. (In Russ.) EDN: TAMTFS
17. Kuraji R, Sekino S, Kapila Y, Numabe Y. Periodontal disease-related nonalcoholic fatty liver disease and nonalcoholic steatohepatitis: An emerging concept of oral-liver axis. *Periodontol 2000*. 2021;87(1):204–240. doi: 10.1111/prd.12387 EDN: HIHGTI
18. Karpishchenko AI. *Clinical laboratory diagnostics of liver and biliary tract diseases: a guide for physicians*. Moscow: GEOTAR-Media; 2020. 464 p. (In Russ.) doi: 10.33029/9704-5256-1-LIV-2020-1-464 EDN: DSHMBZ
19. Orlova SE, Ivanova VA, Degtev IA, et al. Sialometry as a method for diagnosing xerostomia and assessing secretory function (review). *Journal of New Medical Technologies. Electronic Edition*. 2021;15(4):52–57. doi: 10.24412/2075-4094-2021-4-1-9 EDN: SVXOFE
20. Dental Association of Russia. Clinical guidelines (treatment protocols) for the diagnosis "Chronic periodontitis". 2024. Available from: <https://e-stomatology.ru/director/protokols> (In Russ.)

AUTHORS' INFO

***Anna R. Khokhlova**, post-graduate student; North-Western State Medical University named after I.I. Mechnikov; address: 1/82, Zanevsky Ave., Saint Petersburg, 195298, Russia; ORCID: 0009-0001-4790-7377; e-mail: Anna.Khokhlova@szgmu.ru

Natalia S. Robakidze, MD, Dr. Sci. (Medicine), Assistant Professor; ORCID: 0000-0003-4209-5928; eLibrary SPIN: 6653-2182; e-mail: rona24@list.ru

Karina L. Raykhelson, MD, Dr. Sci. (Medicine), Assistant Professor; e-mail: kraikhelson@mail.ru

Margarita V. Klur, MD, Cand. Sci. (Medicine), Assistant Professor; ORCID: 0009-0006-6222-2452; eLibrary SPIN: 8911-6769; e-mail: Margarita.Klur@szgmu.ru

ОБ АВТОРАХ

***Хохлова Анна Робертовна**, аспирант; Северо-Западный государственный медицинский университет им. И.И. Мечникова; адрес: Заневский пр., 1/82, Санкт-Петербург, 195298, Россия; ORCID: 0009-0001-4790-7377; e-mail: Anna.Khokhlova@szgmu.ru

Робакидзе Наталья Серафимовна, д-р мед. наук, доцент; ORCID: 0000-0003-4209-5928 eLibrary SPIN: 6653-2182; e-mail: rona24@list.ru

Райхельсон Карина Леонидовна, д-р мед. наук, доцент; e-mail: kraikhelson@mail.ru.

Клур Маргарита Вилленовна, канд. мед. наук, доцент; ORCID: 0009-0006-6222-2452; eLibrary SPIN: 8911-6769; e-mail: Margarita.Klur@szgmu.ru

* Corresponding author / Автор, ответственный за переписку