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Original study article

The relationship of microbial biodiversity and clinical forms of oral lichen planus: analysis based on 16S rRNA sequencing

Natalya P. Teplyuk[1], Mikhail A. Stepanov[1], Baira Sh. Damdinova[1], Stepan V. Toshchakov[2], Sergrey A. Noskov[2], Nina A. Tutubalina[2]

[1] Sechenov First Moscow State Medical University (Sechenov University), Moscow, Russia;

[2] National Research Centre "Kurchatov Institute", Moscow, Russia

ABSTRACT

BACKGROUND: The composition and changes of microbiota have a significant impact on overall health and the development of various diseases. Of particular relevance is the problem of changes in the oral microbiota in patients with lichen planus of the oral mucosa. Studying the relationship between the composition of the oral microbiota and the pathogenesis of oral lichen planus will improve the understanding of the mechanisms of this disease. Thus, this topic is of considerable interest to a wide range of specialists in the field of medicine and biology.

AIM: Detailed analysis of oral cavity microbiota and establishment of potential pathogenetic microbial associations with oral lichen planus.

MATERIALS AND METHODS: The study included samples from patients diagnosed with various forms of oral red squamous lichen planus (lichen planus erosive-ulcerative) and a control group. The investigation was based on analyzing microbial diversity metrics (alpha and beta diversity), relative abundance of bacterial taxa, and identification of unique bacterial taxa in the oral red squamous lichen planus patients. This analysis utilized the 16S rRNA sequencing method.

RESULTS: The analysis revealed a rich bacterial composition in patients with oral lichen planus, which was significantly different from that in the control group. Differences were also observed between the subgroups, especially between the typical and erosive-ulcerative forms of the disease. Notably, beta diversity did not show significant differences between the groups, indicating a similar overall microbiota composition despite fluctuations in the relative abundance of species. Nevertheless, the typical clinical form of the disease demonstrated more significant differences in the microbiota structure compared to the hyperkeratotic and erosive-ulcerative forms. Furthermore, analysis of the study groups revealed the presence of 50% shared microbial species, while the other half was represented by unique species associated with oral lichen planus. Regarding the subgroups, it was found that unique microorganisms correlated with the typical and erosive-ulcerative forms, respectively, providing a deeper understanding of the specific microbiological profile in the context of this disease.

CONCLUSION: The study confirmed the hypothesis of an association between the microbiota composition and oral lichen planus, which may be of importance for the development of novel therapeutic approaches.

Keywords: oral lichen planus; oral cavity microbiome; alpha diversity; beta diversity; sequencing.

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Оригинальное исследование

Взаимосвязь микробного биоразнообразия и клинических форм красного плоского лишая слизистой оболочки полости рта: анализ на основе 16S рРНК секвенирования

Н.П. Теплюк[1], М.А. Степанов[1], Б.Ш. Дамдинова[1], С.В. Тощаков[2], С.А. Носков[2], Н.А. Тутубалина[2]

[1] Первый Московский государственный медицинский университет имени И.М. Сеченова (Сеченовский Университет), Москва, Россия;

[2] Национальный исследовательский центр «Курчатовский институт», Москва, Россия

АННОТАЦИЯ

Обоснование. Состав и изменения микробиоты могут оказывать существенное влияние на общее состояние здоровья и развитие различных заболеваний. Особую актуальность представляет проблема изменения микробиоты полости рта у пациентов с красным плоским лишаём слизистой оболочки полости рта. Изучение взаимосвязи патогенеза заболевания с составом микрофлоры полости рта позволит улучшить понимание механизмов развития патологии и разработать терапевтический подход к её лечению. Таким образом, данная тема представляет значительный интерес для широкого круга специалистов в области медицины и биологии.

Цель исследования — детальное изучение состава микробиоты полости рта у пациентов с красным плоским лишаём слизистой оболочки полости рта для выявления возможных патогенетических микробных ассоциаций.

Материалы и методы. В исследование включены образцы мазков с поверхности слизистой оболочки рта для секвенирования ДНК от пациентов с различными формами красного плоского лишая и контрольной группы. Исследование основано на анализе показателей разнообразия микробиоты (альфа- и бета-разнообразие; относительное содержание бактериальных таксонов; выявление уникальных бактериальных таксонов). Для исследования использован метод секвенирования 16S РНК.

Результаты. Анализ выявил многообразный бактериальный состав у пациентов с красным плоским лишаём слизистой оболочки полости рта, который существенно отличается от контрольной группы, а также различия между подгруппами, особенно при типичной и эрозивно-язвенной формах заболевания. Стоит отметить, что бета-разнообразие не показало значимых различий между группами, что указывает на сходный общий состав микробиоты, несмотря на колебания в относительной численности видов. Тем не менее типичная клиническая форма заболевания демонстрирует более существенные различия в структуре микробиома по сравнению с гиперкератотической и эрозивно-язвенной формами. Более того, анализ исследуемых групп позволил установить наличие 50% общих видов микроорганизмов, а другая половина представлена уникальными видами, ассоциированными с красным плоским лишаём слизистой оболочки полости рта. В отношении подгрупп выявлено, что уникальные микроорганизмы коррелируют с типичной и эрозивно-язвенной формами соответственно, предоставляя тем самым более глубокое понимание специфики микробиологического профиля в контексте данного заболевания.

Заключение. Исследование подтвердило гипотезу о связи состава микробиоты полости рта с красным плоским лишаём слизистой оболочки полости рта, что может иметь важное значение для разработки новых терапевтических подходов.

Ключевые слова: красный плоский лишай слизистой оболочки полости рта; микробиом; альфа-разнообразие; бета-разнообразие; секвенирование.

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ЭКО•ВЕКТОР

BACKGROUND

Lichen planus (LP) of the oral mucosa (OLP) is a chronic inflammatory disease of the oral mucosa (OM) of unknown etiology. It is characterized by inflammation, erosion, and damage to the stratified squamous epithelium and the OM connective tissue plate, sometimes accompanied by skin and nail damage [1].

In the Russian Federation, the incidence of LP among the population aged >18 years has reached 12.7 per 100 thousand people. LP most often occurs in people aged 30–60 years. Women account for 60%–75% among patients with OM lesions, and approximately 50% among patients with skin lesions [2].

LP of the OM and vermilion surface manifests in six clinical forms, namely, typical (reticular), hyperkeratotic, exudative-hyperemic, erosive-ulcerative, bullous, and atypical [3, 4].

Contemporary research of the OLP is increasingly recognizing the role of the oral microbiome and its interaction with the environment of the host organism. This is attributed to the importance of the human microbiota in the development of various diseases, making the regulation of microbiocenosis a key aspect of personalized medicine [5].

Various microorganisms have been studied as potential factors associated with OLP development, including *Helicobacter pylori, Mycoplasma salivarium*, periodontopathogenic bacteria, *Candida albicans*, human papillomavirus, Epstein–Barr virus, and hepatitis C virus. However, data on such associations are controversial and require further investigations. Existing studies reported conflicting results, and the mechanisms underlying these relationships are not fully understood [4].

Despite studies searching for specific OLP-associated microorganisms, a clear correspondence between their presence and disease development has not been revealed. This suggests the more significant role of the functional characteristics of the oral microbiota in the pathogenesis of OLP than its species composition. Currently, no microorganism can be recognized as the cause of this disease [5].

In this study, the 16S rRNA-sequencing method was used, which enabled the assessment of the biodiversity of microorganisms in patients with OLP. The microbial composition in patients with OLP was compared with those of the control group, followed by pairwise comparisons of the microbiota in different disease forms (typical, erosive-ulcerative, and hyperkeratotic). Thus, the microbial profile was characterized for each clinical form, and unique microbial signatures associated with each type of the disease were identified.

This study aimed to analyze comprehensively the oral microbiota composition in patients with OLP to identify possible pathogenetic microbial associations.

MATERIALS AND METHODS

Study design

The study employed a cross-sectional one-stage design.

Compliance criteria

The *inclusion criteria* were as follows: OLP diagnosis established earlier or for the first time; voluntary participation, provision of written informed consent for study participation, and consent to the processing of personal data; age ⩾18 years; patients of different sexes; non-intake of systemic antibiotics 30 days before and application of topical agents 3 days before sample collection.

The *non-inclusion criteria* were as follows: failure to meet the inclusion criteria, history of severe concomitant pathology or other autoimmune diseases, and patient's reluctance to participate in the study.

The exclusion criteria were as follows: the patient's desire to discontinue participation in the study and non-compliance to the regimen, prescribed examination, and treatment schedule.

Conditions

The study was conducted at the V.A. Rakhmanov Clinic of Skin and Sexually Transmitted Diseases of the Sechenov University (Moscow) and the National Research Center "Kurchatov Institute" (Moscow).

Study duration

The study was conducted from January 2022 to November 2023.

Methods of outcome registration

A comparative study of the OM microbiota was performed by DNA-sequencing in groups. The main group consisted of 45 patients with OLP, and the control group consisted of 40 patients with other diseases of the OM, including 15 patients with pemphigus vulgaris, 10 with recurrent oral ulceration, and 15 with leukoplakia. Depending on the clinical disease form, the main group was divided into four subgroups, namely, typical (n = 9), hyperkeratotic (n = 17), erosive-ulcerative (n = 17), and exudative-hyperemic (n = 2) groups. In the exudative-hyperemic subgroup, owing to the small sample size, a comparative study of the OM microbiota was not conducted.

Sequencing resulted in 7956–121,460 reads per sample. After filtering and removing chimeric sequences, the analysis included 4,874–68,898 reads per sample. Data were processed in the R programming language (v 4.2.0) using the dada2 package (v 1.24.0). A rarefaction curve of amplicon sequence variants (ASV) was plotted, and most samples became saturated at 10,000 reads.

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For the ecological analysis of the buccal epithelium microbiome in the oral cavity, the following methods were used:

• Alpha diversity using the estimate_richness function of the phyloseq package (v 1.40.0): the significance of the between-group difference was determined by the Wilcoxon T-test, and the null hypothesis was rejected at p-value < 0.05.

• Beta diversity using the cal_betadiv function of the microeco package (v 0.19.5): compositional dissimilarities between groups were considered Bray–Curtis dissimilarity, and the significance of group differences was determined using PERMANOVA.

• Representation analysis, differential analysis of representation, and Venn analysis were calculated in the microeco package (v 0.19.5).

Ethical considerations

The study was approved by the local ethics committee of Sechenov University (Protocol No. 01-22 of 01/20/2022). All patients provided signed voluntary informed consent to participate in the study. The patients were fully informed about the study, therapy courses, possible outcomes, and side effects of the therapy.

Statistical analysis

IBM SPSS Statistics version 27.0 (IBM Corp., Armonk, NY, USA) was used to perform statistical analysis. Descriptive statistics included the calculation of means and standard deviations for quantitative data and frequencies and percentages for categorical data. The R programming language (v 4.2.0) was used to analyze DNA-sequencing data by employing the dada2 (v 1.24.0) and phyloseq (v 1.40.0) packages. A p-value of <0.05 was considered significant.

RESULTS

Objects (participants) of the study

The main group consisted of 45 patients with OLP [10 (22.22%) men, 35 (77.78%) women; average age, 55.3 ± 13.4 years]. The control group consisted of 40 patients with other OM diseases, including 15 patients with pemphigus vulgaris, 10 with recurrent oral ulceration, and 15 with leukoplakia. The study revealed significant differences between the groups. The main group had significantly higher proportion of women (77.7% versus 55% in the control group, $p < 0.05$) and higher prevalence of smoking (33.3% vs. 10%, $p < 0.05$); gastritis associated with *H. pylori* (22.2% vs. 10%, $p < 0.05$), type 2 diabetes mellitus (33.3% vs. 2.5%, $p < 0.05$), and obesity (22.2% vs. 2.5%, $p < 0.05$) (Table 1).

Main research results

Alpha diversity analysis. The bacterial composition was more diverse in the samples of the main group (Fig. 1); however, when comparing different OLP forms, significant differences were revealed for the typical and erosive-ulcerative forms when using the Chao1 and Shannon indices in the control group samples (Fig. 2).

The rarefaction curves indicated that the results represented virtually the entire bacterial population in

Table 1. Main characteristics of patients with red squamous lichen planus of the oral mucosa

Parameter	Group		*p*
	Main, *n*=45	Control, *n*=40	
Sex			
• Male	10 (22.2)	8 (20)	-
• Female	**35 (77.7)**	22 (55)	
Age, years, M ± m	55.3±13.4	53.7±11.9	>0.05
Type:			
• Typical	17 (37.7)	-	-
• Erosive-ulcerative	17 (37.7)	-	-
• Hyperkeratotic	9 (20)	-	-
• Exudative-hyperemic	2 (4.4)	-	-
Smoking	**15 (33.3)**	**4 (10)**	**<0.05**
Gastritis associated with *H. pylori*	**10 (22.2)**	**4 (10)**	**<0.05**
Chronic esophagitis	2 (4.4)	1 (2.5)	>0.05
Hypertonic disease	15 (33.3)	10 (25)	>0.05
Type 2 diabetes mellitus	**15 (33.3)**	**1 (2.5)**	**<0.05**
Obesity	**10 (22.2)**	**1 (2.5)**	**<0.05**

Note. Significant differences between the main and control groups with p <0,05 are highlighted in bold.

samples taken from the main group, as indicated by the 97% Good's coverage (Fig. 3).

Analysis of representation. An analysis of the 10 most common taxa showed that in the main group, the relative amounts of bacteria at the level of phyla *Actinobacteria, Bacteroidota,* and *Fusobacteria* (Fig. 4*a*), families *Pasteurellaceae* and *Pseudomonadaceae* (Fig. 5*a*), and genera *Pseudomonas* and *Porphyromonas* increased. A wide range of other genera was also recorded (Fig. 6*a*). In addition, the bacterial populations of the phyla *Firmicutes* and *Proteobacteria* (Fig. 4*a*), families *Streptococcaceae*, *Gemellaceae* and *Carnobacteriaceae* (Fig. 5*a*), and genera *Streptococcus, Granulicatella,* and *Gemella* decreased (Fig. 6*a*). Note that in the erosive-ulcerative and hyperkeratotic OLP, the *Streptococcus* population decreased compared with other clinical variants of the disease (Fig. 6*b*). The significance of the data obtained was confirmed using the Wilcoxon test ($p < 0.05$).

Beta diversity analysis. The calculation of beta diversity did not reveal any differences between the main group and the control group (Fig. 7); however, when compared by disease form, significant differences were recorded (Fig. 8). In particular, the typical and hyperkeratotic forms were clearly grouped (Fig. 8*b*), as well as the erosive-ulcerative and hyperkeratotic forms (Fig. 8*d*) with *p* values of 0.628 and 0.612, respectively. This finding suggests that the typical form demonstrates more significant differentiation in the structure

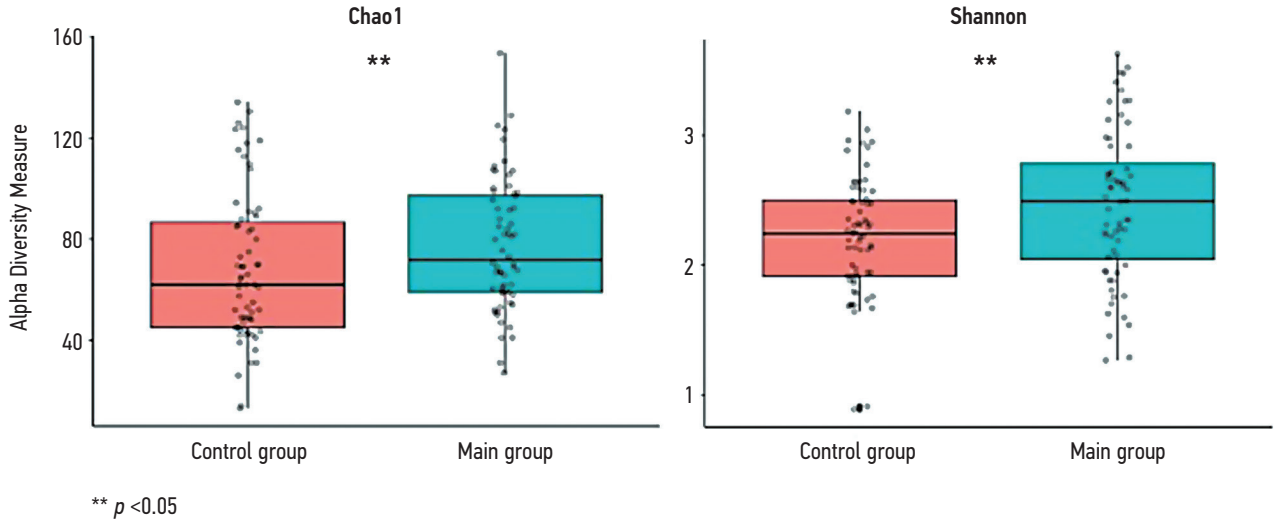

Fig. 1. Analysis of alpha diversity of the bacterial composition of the oral mucosa depending on the presence of the disease using the Chao1 and Shannon indices.

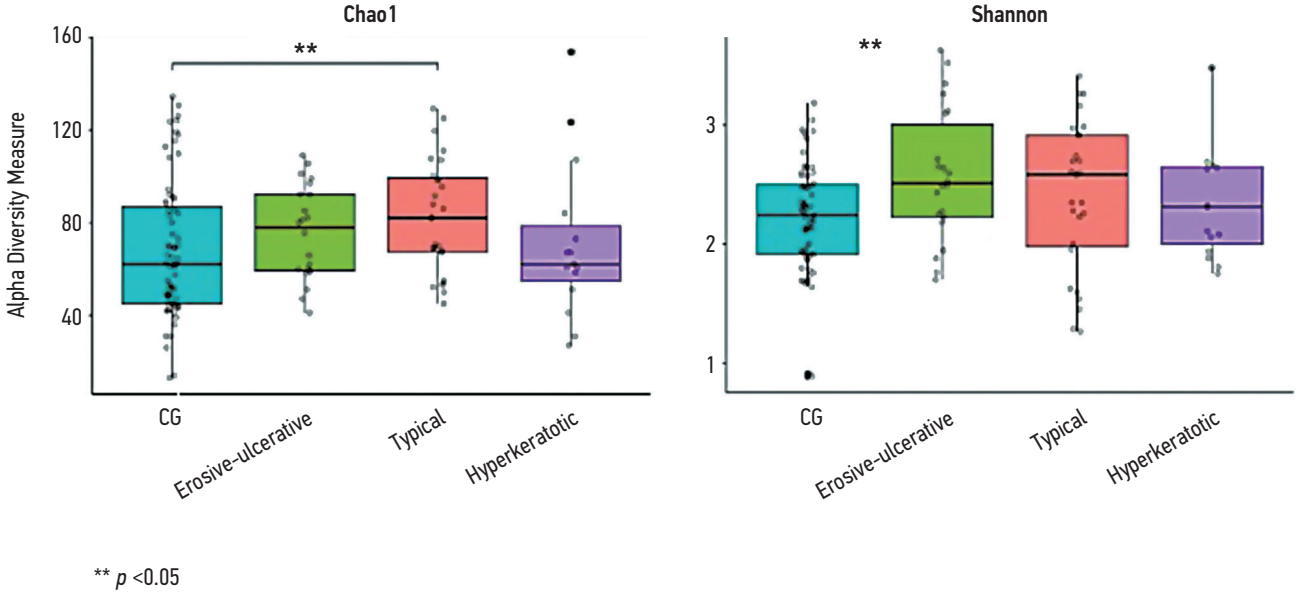

Fig. 2. Alpha diversity measurement of bacterial composition of oral cavity according to the form of the oral lichen planus disease using Chao1 and Shannon Index.

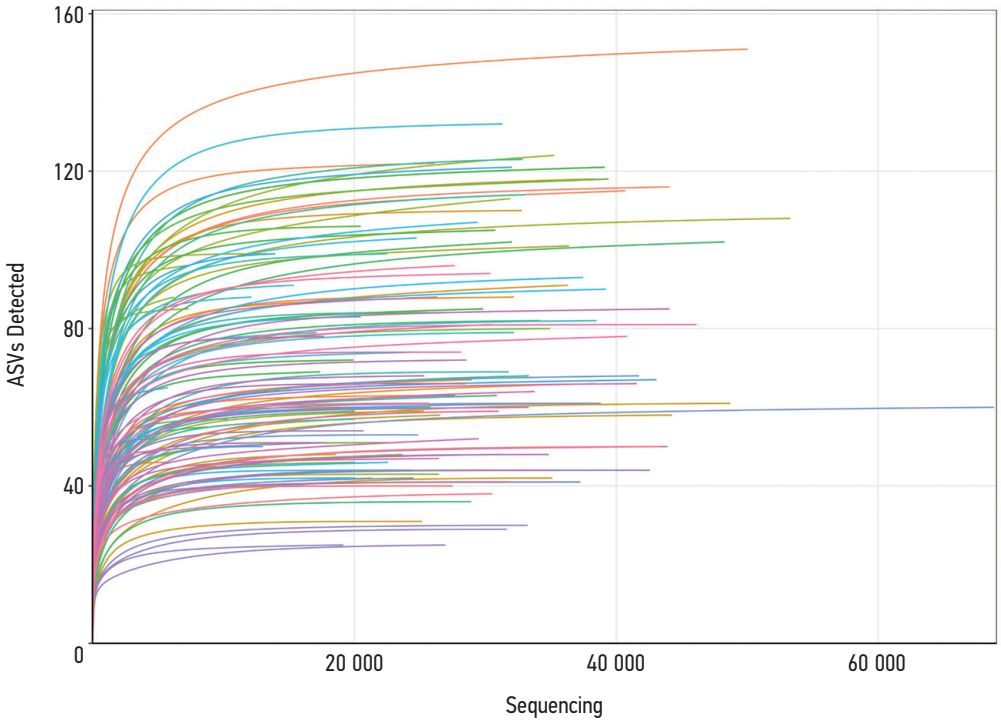

Fig. 3. Rarefaction curve plot.

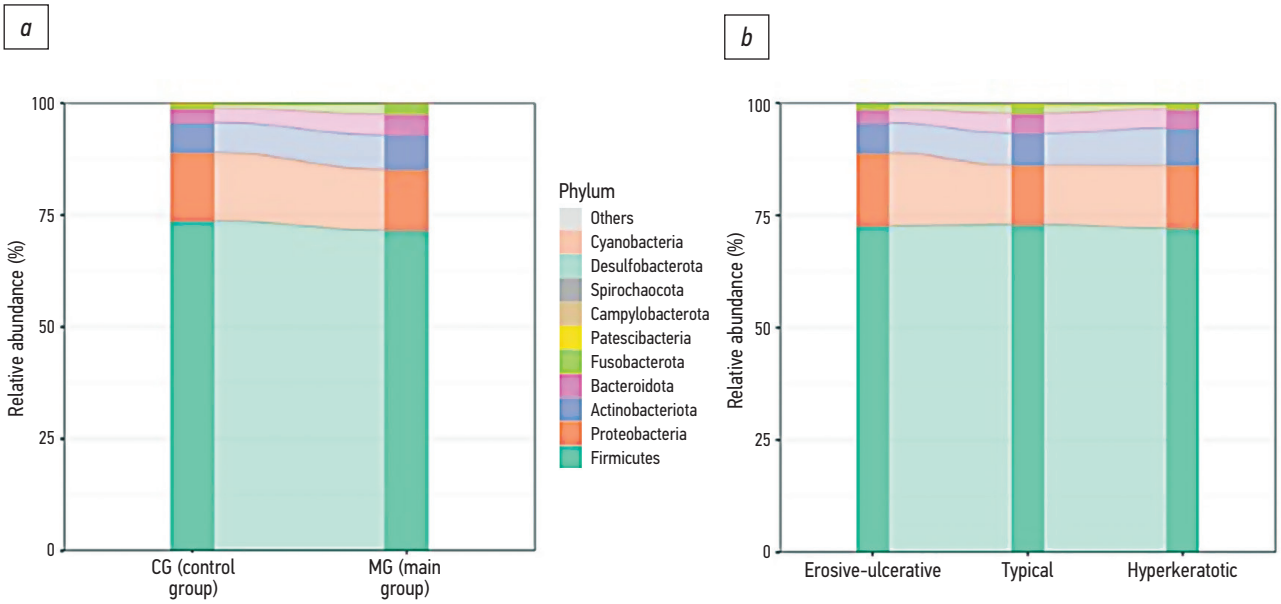

Fig. 4. Representation of the relative abundance of oral microbiota at the phylum level with comparisons between the main group (MG) and control group (CG) (*a*), as well as among the typical, erosive-ulcerative, and hyperkeratotic forms (*b*) (The 10 more frequent taxa).

of the microbiome compared with the hyperkeratotic and erosive-ulcerative forms.

Venn analysis. This analysis provided information about overlapping and unique ASVs in the groups analyzed. Only half of the ASV overlapped between the main and control groups (Fig. 9*a*). When comparing disease types, the hyperkeratotic form differed most significantly from the microbiome of the control group, and it also differed from other forms (Fig. 9*b*).

Analysis of differential representation. Compared with the control group, the main group exhibited significant differences in the number of nine unique species of microorganisms of various taxonomic levels (Fig. 10). In addition, a comparative analysis of the microbiota by clinical forms revealed diversity in species composition between the hyperkeratotic and typical forms, highlighting the specific microbial profile of each form (Fig. 11).

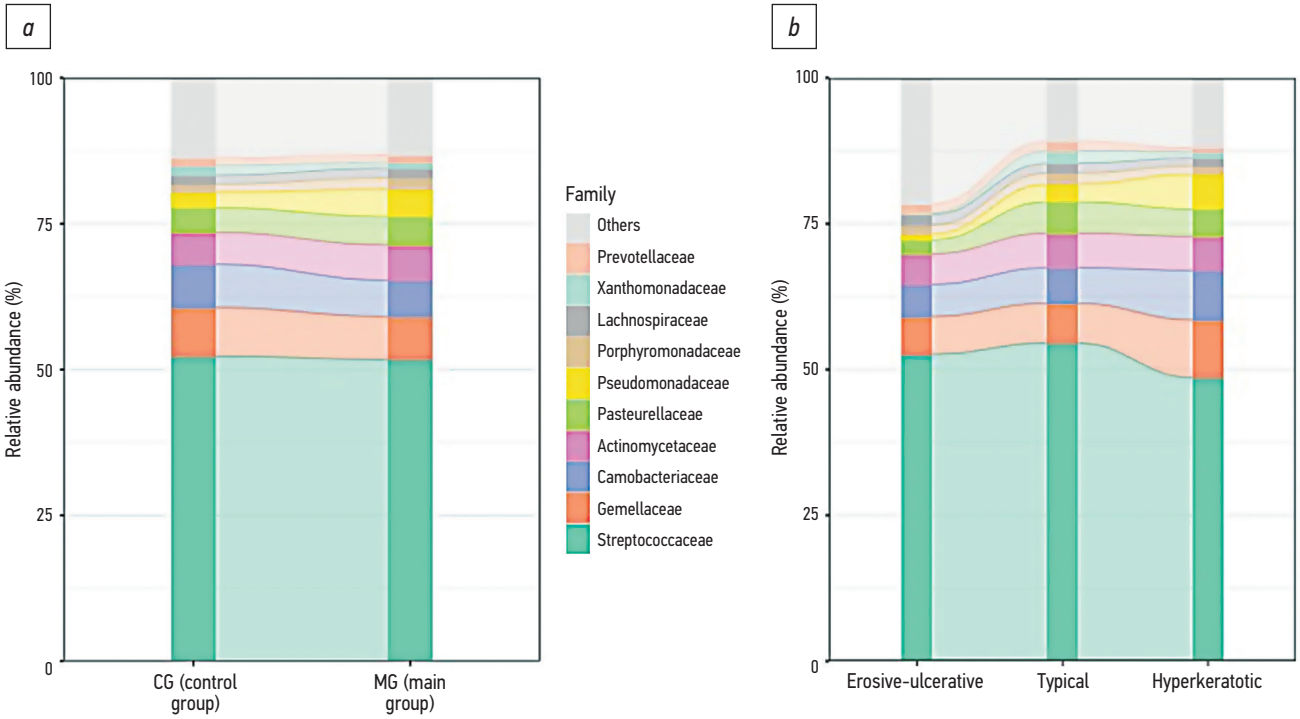

Fig. 5. Representation of the relative abundance of oral microbiota at a family level with comparisons between the main group (MG) and control group (CG) (*a*), as well as among the typical, erosive-ulcerative, and hyperkeratotic forms (*b*) (The 10 more frequent taxa).

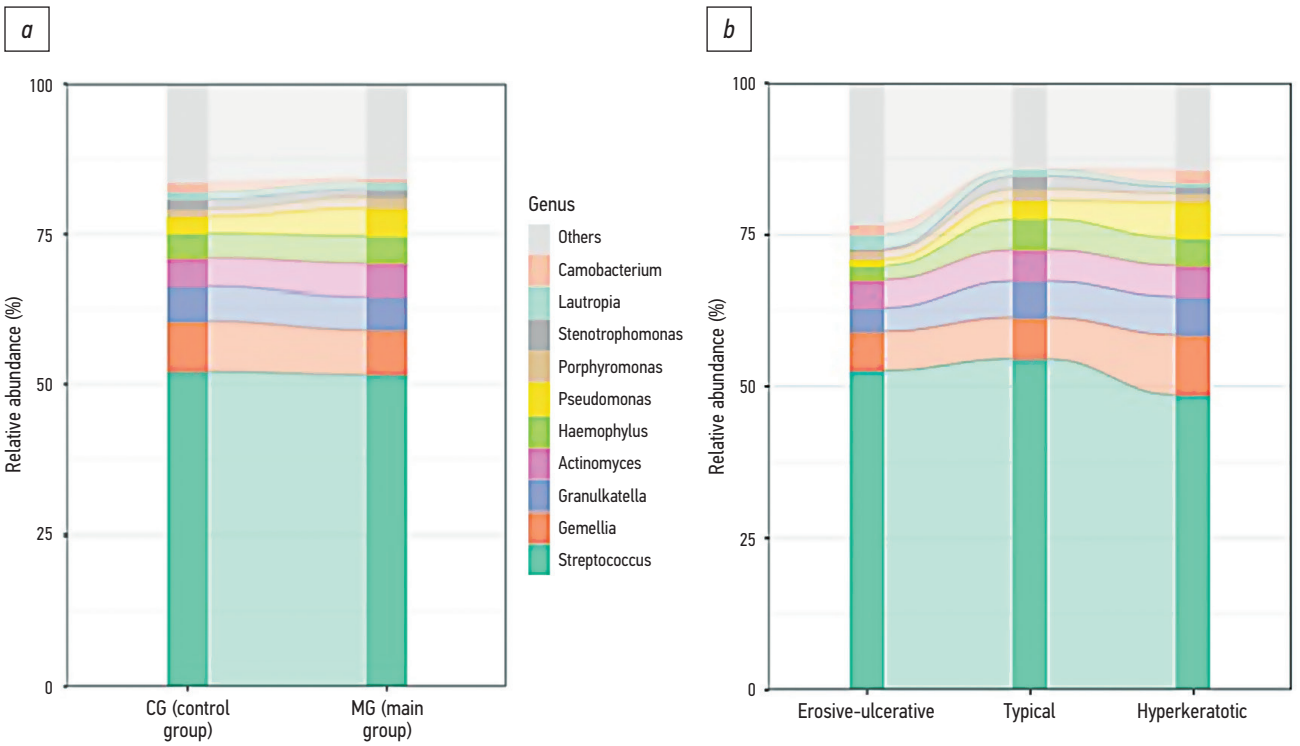

Fig. 6. Representation of the relative abundance of oral microbiota at a genus level with comparisons between the main group (MG) and control group (CG) (*a*), as well as among the typical, erosive-ulcerative, and hyperkeratotic forms (*b*) (The 10 more frequent taxa).

DISCUSSION

In this study, the microbial composition in patients with OLP was analyzed, and the results were compared with the indicators of the control group. Differences in microbial composition depending on the clinical forms (typical, erosive-ulcerative, and hyperkeratotic) were also examined, which enabled detailed comparative analysis of the subgroups.

The results of alpha diversity analysis (Fig. 1) showed a more diverse microbial composition in the main group.

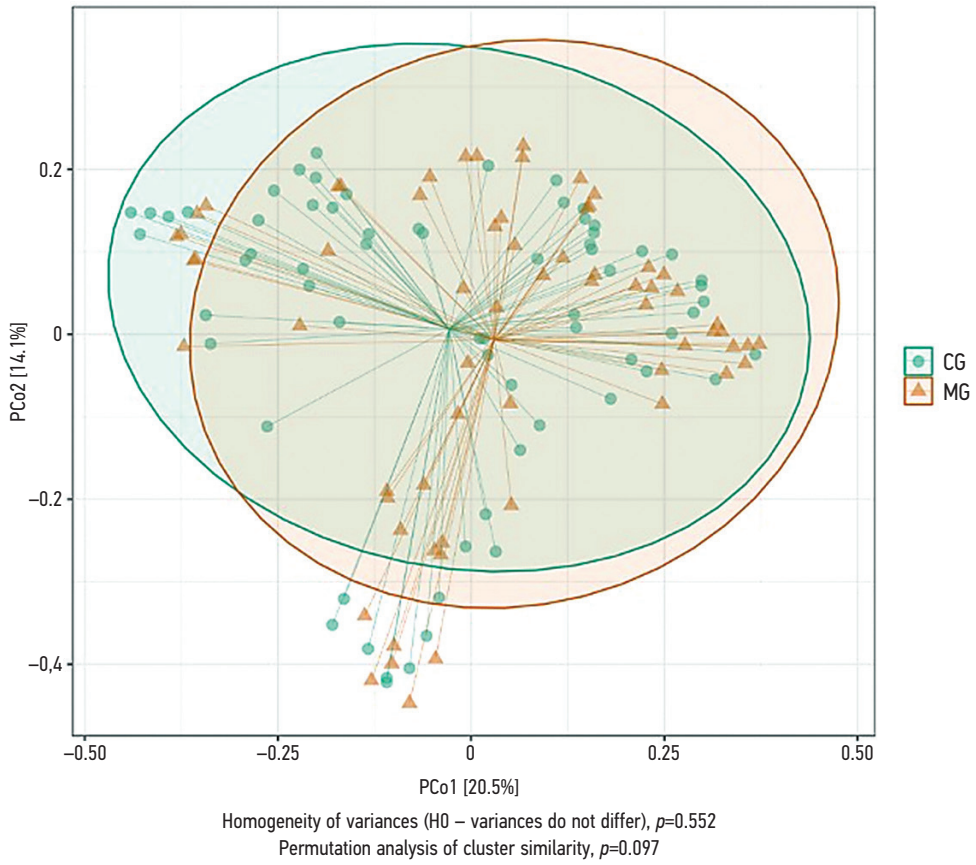

Fig. 7. Beta-diversity analysis of microbial community compositional differences between the main group (MG) and the control group (CG) using PCoA (Principal coordinate Analysis).

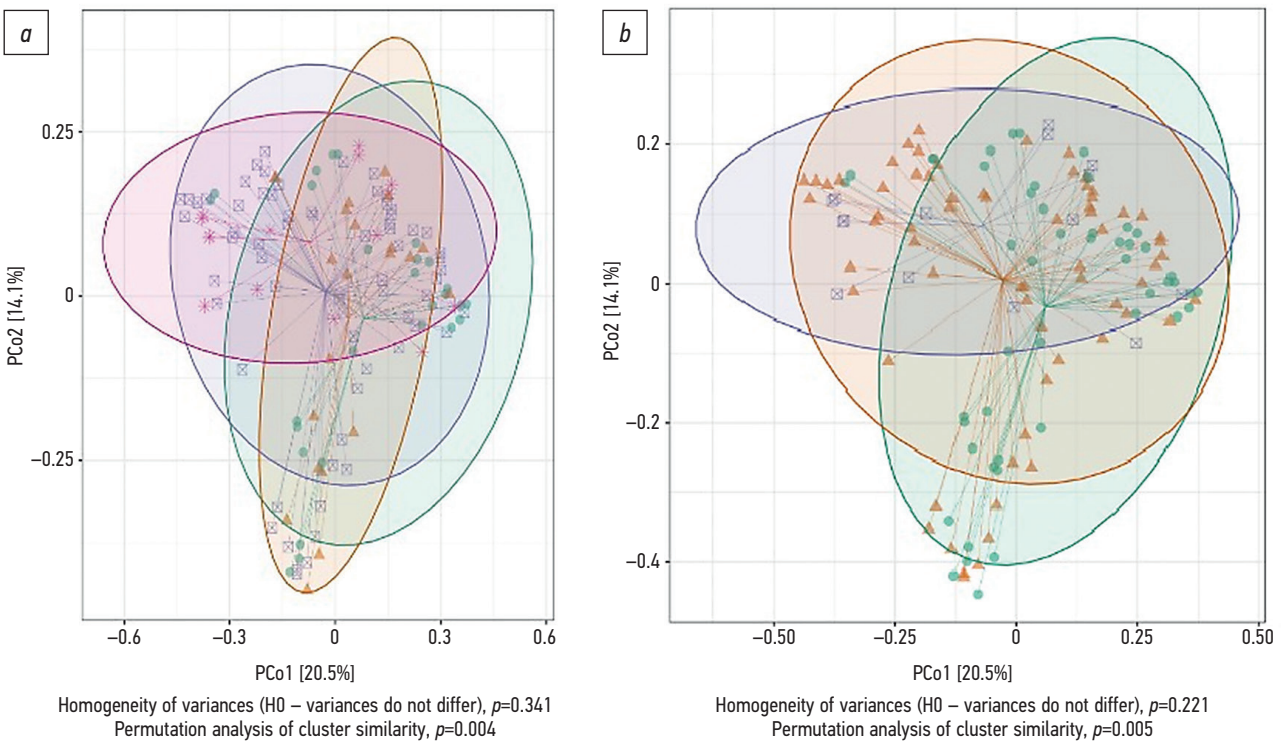

Fig. 8. Beta-Diversity Analysis of microbial community compositional differences according to the form of the disease using PCoA (Principal coordinate Analysis).

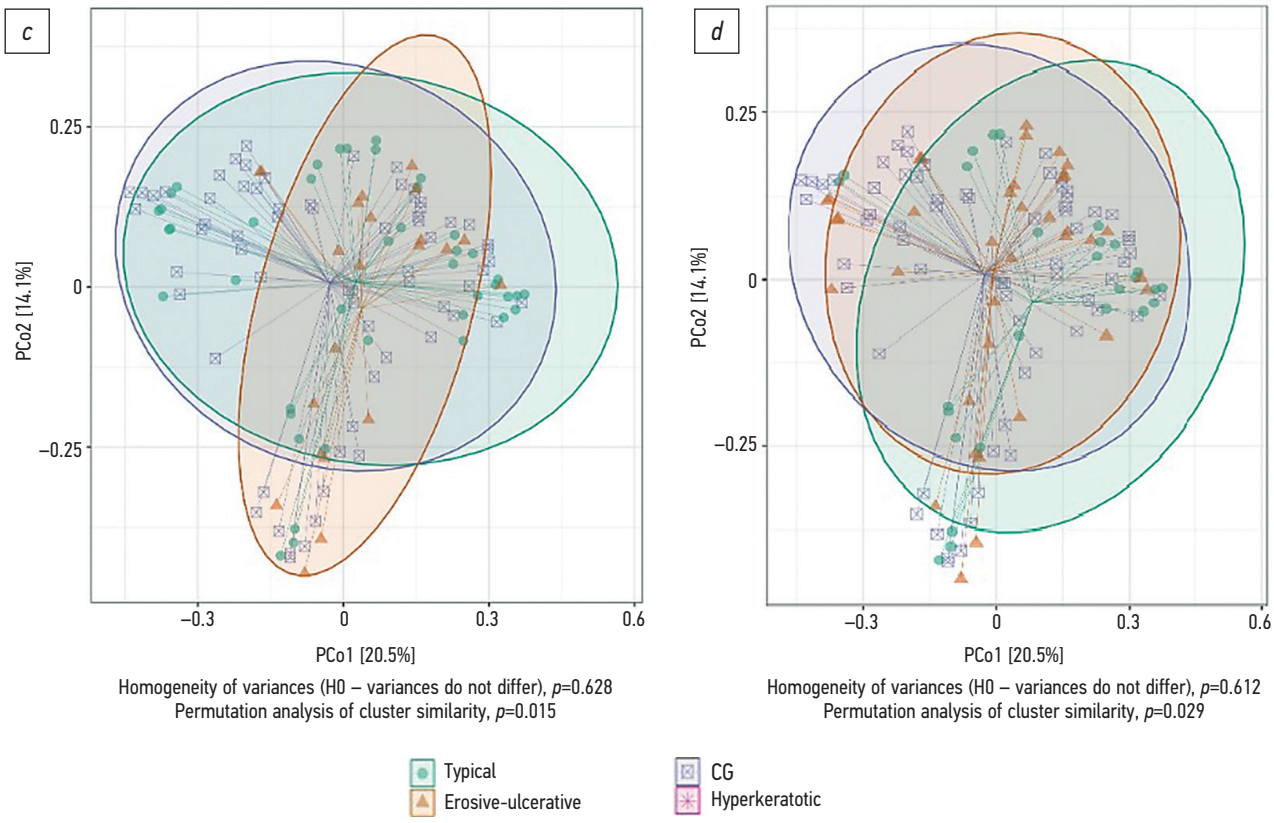

Fig. 8. Ending.

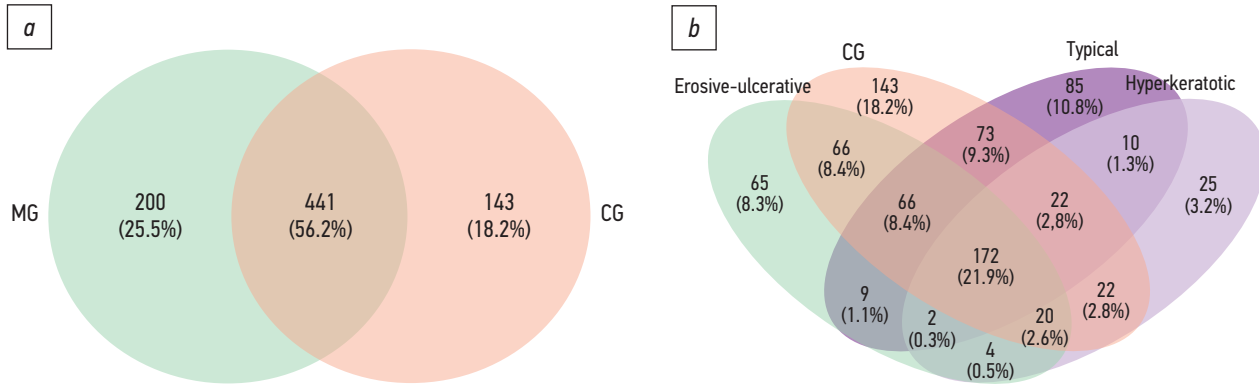

Fig. 9. Venn diagram representation of the main (MG, oral lichen planus patients) and control (CG) group (*a*) and according to clinical form (*b*).

Moreover, a comparison of various clinical forms of OLP in the main group with the indicators of the control group revealed significant differences in the biodiversity of microorganisms, particularly the typical and erosive-ulcerative forms, which is confirmed by Chao1 and Shannon indices (Figs. 4–6). The present results differ from those of F.Y. Yu et al. [6]. The differences may be caused by the specific composition of the control group, diversity of sequenced regions, and other confounders that can modify the relationship between the risk factor in question and the study outcome.

The relative abundance of the oral microbiota at all taxonomic levels (phylum, family, and genus) also showed that the dominant bacteria in OLP were significantly different from those detected in the control group. The subgroup analysis of the relative abundance revealed that the *Streptococcus* population was lower in erosive-ulcerative and hyperkeratotic forms than in the typical form. On the contrary, M.M. Bornstein et al. [7] reported that in patients with LP having nonerosive/asymptomatic lesions, the bacterial loads for *Capnocytophaga sputigena*, *Eikenella corrodens*, *Lactobacillus crispatus*, *Mobiluncus curtisii*,

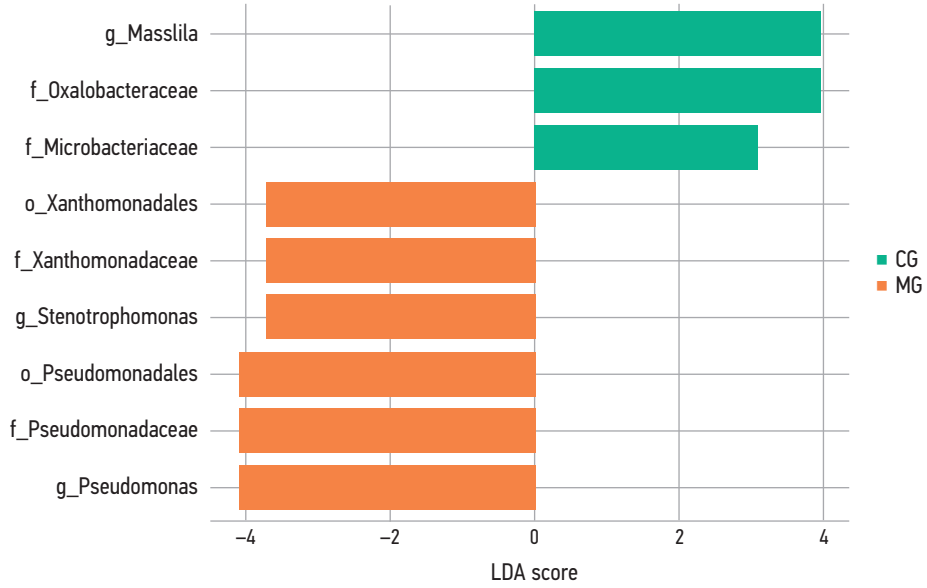

Fig. 10. Differential abundance of amplicon sequence variants (ASV) between the main group (MG) and the control group (CG) as determined by linear discriminant analysis (LDA).

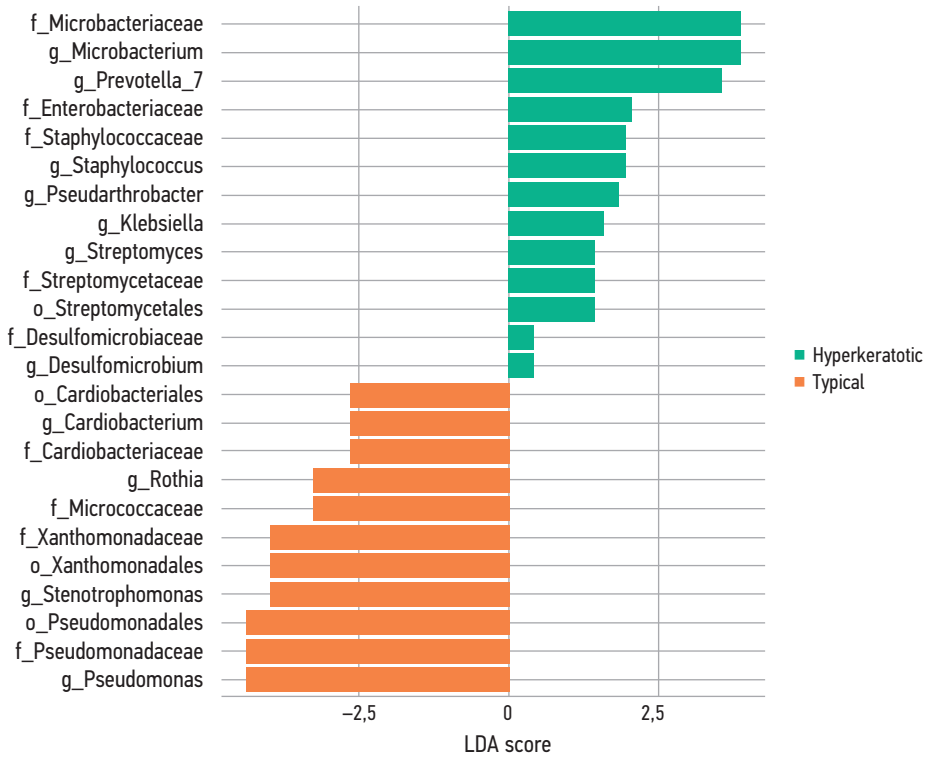

Fig. 11. Differential abundance of amplicon sequence variants (ASVs) between the typical and hyperkeratotic forms of oral lichen planus using linear discriminant analysis (LDA).

Neisseria mucosa, *Prevotella bivia*, *Prevotella intermedia*, and *Streptococcus agalactiae* in the LP lesion were significantly higher than those in similar sites of the control group. However, this discrepancy may be due to the analysis of asymptomatic patients, which implies the exclusion of the influence of oral hygiene, which can introduce differences in the species composition of microorganisms [8].

The results also confirm that the microbiota of both groups, despite the presence of numerous ulcers of the OM, differs distinctly. This finding suggests that changes in the oral microbiota may be directly related to the underlying pathological process and not only to the presence of oral ulcers or the inflammatory environment in the oral cavity.

The microbial composition of the main group was significantly different from that of the control group. Increased amounts of periodontitis-associated pathogens such as *Pseudomonas* and *Porphyromonas* in the main group compared with the control group were notable, which indicated the significant difference in the microbial ecosystem (Figs. 4–6).

This study confirms the results of previous studies that assessed the prevalence of periodontal pathogens using culture methods. However, in contrast to a previous study, where the control group consisted of patients without OLP but had periodontitis or gingivitis, the control group of the present study did not have any oral diseases. Owing to this selection of a control group, microorganisms with periodontal destructive effects were detected, namely, *Aggregatibacter actinomycetemcomitans*, *Veillonella parvula*, *Porphyromonas gingivalis,* and *Treponema denticola,* which can be associated with OLP [8].

In contrast to alpha diversity measures, which demonstrated differences in the oral microbiota of the main group compared with the control group, the analysis of beta diversity did not reveal significant differences between the groups. Thus, while the microbiota composition (beta diversity) remains essentially similar between the study groups, the diversity and abundance of individual species (alpha diversity) differ, indicating specific changes in the microbial community, associated with oral health.

This phenomenon can be interpreted by the presence of certain conditions that may promote the growth of specific bacteria existing in the oral cavity. These bacterial species then increase in abundance, whereas others may decrease, resulting in a change in alpha diversity without a marked change in the overall spectrum of bacteria present.

A pairwise comparison of beta diversity indices between the subgroups showed that samples from the typical subgroup were characterized by a more pronounced difference in the microbiota composition compared with the samples from the hyperkeratotic and erosive-ulcerative subgroups. These differences in microbial composition among clinical forms suggest that changes in the oral microbiota not only precede the development of more severe forms but may also influence actively such forms and severity.

Venn diagrams revealed significant similarity in the microflora between the control and main groups, confirming the results of previous beta diversity analysis. However, the presence of unique microorganisms in patients with the disease emphasizes their specific role and indicates a distinct microbiome signature associated with this condition.

Detailed (linear discriminant) analysis revealed unique bacterial taxa characteristic of the main group; thus, *Pseudomonas, Pseudomonadaceae,* and *Pseudomonadales* deserve special attention because of their high ecological resistance and potential for opportunistic pathogenicity. The increase in their abundance in patients with OLP suggests possible pathogenic changes in the oral microbiota composition [9]. *Stenotrophomonas, Xanthomonadaceae*, and *Xanthomonadales* are also of concern because of antibiotic resistance and infections, which, given their dominance in the main group, indicates dysbiosis associated with the disease [10]. Finally, *Massilia, Oxalobacteraceae,* and *Microbacteriaceae*, which are less dominant in the oral cavity, may represent commensal bacteria characteristic of a healthy oral microbiome.

The subgroup analysis using linear discriminant analysis identified certain bacterial taxa with significantly different abundances between hyperkeratotic and typical forms, consistent with beta diversity.

CONCLUSION

Changes in the oral microbiota composition may be of key importance in the pathogenesis of OLP, indicating the relationship between microbial imbalance and disease development. Moreover, the discovery of high pathogen load associated with periodontal diseases emphasizes the possible overlap of pathogenetic mechanisms between OLP and periodontitis, which opens up prospects for further study of their relationship. In addition, the unique microbial signatures that are associated with various clinical forms of OLP offer a basis for the development of targeted therapeutic approaches. This approach can contribute to the creation of differentiated treatment strategies adjusted to the specifics of each clinical form.

The importance of additional research to clarify the cause-and-effect relationships between microbiota changes and OLP cannot be overemphasized. A thorough understanding of these relationships may be the key to the development of personalized approaches to OLP treatment and prevention, which will ultimately increase the treatment efficiency and the quality of life of patients.

ADDITIONAL INFORMATION

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REFERENCES

1. Roopashree MR, Gondhalekar RV, Shashikanth MC, et al. Pathogenesis of oral lichen planus: A review. *J Oral Pathol Med.* 2010;39(10):729–734. doi: 10.1111/j.1600-0714.2010.00946.x
2. *Federal clinical recommendations for the management of patients with red squamous lichen planus.* Moscow: Russian Society of Dermatovenerologists and Cosmetologists, 2015. 19 p. (In Russ).
3. Chuykin SV, Akmalova GM, Chernysheva ND. Clinical features of lichen ruber planus of the oral mucosa. *Russ J Clin Dermatol Venereol.* 2015;14(3):72–75. doi: 10.17116/klinderma201514372-75
4. Teplyuk NP, Stepanov MA, Damdinova BSh, Lazareva PI. Etiology, clinical manifestations, and oral microbiota in oral lichen planus: A review of the scientific literature. *Russ J Skin Venereal Dis.* 2023;26(6):553–562. EDN: IMYRHA doi: 10.17816/dv569013
5. Jung W, Jang S. Oral Microbiome research on oral lichen planus: Current findings and perspectives. *Biology.* 2022;11(5):723. doi: 10.3390/biology11050723
6. Yu FY, Wang QQ, Li M, et al. Dysbiosis of saliva microbiome in patients with oral lichen planus. *BMC Microbiol.* 2020;20(1):75. doi: 10.1186/s12866-020-01733-7
7. Bornstein MM, Hakimi B, Persson GR. Microbiological findings in subjects with asymptomatic oral lichen planus: A cross-sectional comparative study. *J Periodontol.* 2008;79(12):2347–2355. doi: 10.1902/jop.2008.080303
8. Svitich OA, Teplyuk NP, Stepanov MA, et al. Studying the relationship between oral lichen planus and periodontal disease: Value on periodontal pathogens and oral hygiene. *Russ J Clin Dermatol Venereol.* EDN: CKPMVN 2024;27(1):45–54. doi: 10.17816/dv624269
9. Zaatout N. Presence of non-oral bacteria in the oral cavity. *Arch Microbiol.* 2021;203(6):2747–2760. doi: 10.1007/s00203-021-02300-y
10. Brooke JS. Stenotrophomonas maltophilia: An emerging global opportunistic pathogen. *Clin Microbiol Rev.* 2012;25(1):2–41. doi: 10.1128/CMR.00019-11

СПИСОК ЛИТЕРАТУРЫ

1. Roopashree M.R., Gondhalekar R.V., Shashikanth M.C., et al. Pathogenesis of oral lichen planus: A review // J Oral Pathol Med. 2010. Vol. 39, N 10. P. 729–734. doi: 10.1111/j.1600-0714.2010.00946.x
2. *Федеральные клинические рекомендации по ведению больных красным плоским лишаем.* Москва: Российское общество дерматовенерологов и косметологов, 2015. 19 с.
3. Чуйкин С.В., Акмалова Г.М., Чернышева Н.Д. Особенности клинического течения красного плоского лишая с локализацией на слизистой оболочке полости рта // Клиническая дерматология и венерология. 2015. Т. 14, № 3. С. 72–75. doi: 10.17116/klinderma201514372-75
4. Теплюк Н.П., Степанов М.А., Дамдинова Б.Ш., Лазарева П.И. Этиология, клинические проявления и микробиота красного плоского лишая слизистой оболочки полости рта: обзор научной литературы // Российский журнал кожных и венерических болезней. 2023. Т. 26, № 6. С. 553–562. EDN: IMYRHA doi: 10.17816/dv569013
5. Jung W., Jang S. Oral microbiome research on oral lichen planus: Current findings and perspectives // Biology. 2022. Vol. 11, N 5. P. 723. doi: 10.3390/biology11050723
6. Yu F.Y., Wang Q.Q., Li M., et al. Dysbiosis of saliva microbiome in patients with oral lichen planus // BMC Microbiol. 2020. Vol. 20, N 1. P. 75. doi: 10.1186/s12866-020-01733-7
7. Bornstein M.M., Hakimi B., Persson G.R. Microbiological findings in subjects with asymptomatic oral lichen planus: A cross-sectional comparative study // J Periodontol. 2008. Vol. 79, N 12. P. 2347–2355. doi: 10.1902/jop.2008.080303
8. Свитич О.А., Теплюк Н.П., Степанов М.А., и др. Изучение взаимосвязи между красным плоским лишаем слизистой оболочки полости рта и заболеваниями пародонта: значение микробиоты пародонтальных патогенов и гигиены полости рта // Российский журнал кожных и венерических болезней. 2024. Т. 27, № 1. С. 45–54. EDN: CKPMVN doi: 10.17816/dv624269
9. Zaatout N. Presence of non-oral bacteria in the oral cavity // Arch Microbiol. 2021. Vol. 203, N 6. P. 2747–2760. doi: 10.1007/s00203-021-02300-y
10. Brooke J.S. Stenotrophomonas maltophilia: An emerging global opportunistic pathogen // Clin Microbiol Rev. 2012. Vol. 25, N 1. P. 2–41. doi: 10.1128/CMR.00019-11

AUTHORS' INFO

*** Baira Sh. Damdinova;**
address: 8-2 Trubetskaya street, 119992 Moscow, Russia;
ORCID: 0000-0002-4162-2928;
e-mail: baira_d@mail.ru

Natalya P. Teplyuk, MD, Dr. Sci. (Med.), Professor;
ORCID: 0000-0002-5800-4800;
eLibrary SPIN: 8013-3256;
e-mail: teplyukn@gmail.com

Mikhail A. Stepanov, MD, Cand. Sci. (Med.), Associate Professor;
ORCID: 0000-0002-1872-9487;
eLibrary SPIN: 6524-5665;
e-mail: Doctor.stepanov@gmail.com

ОБ АВТОРАХ

*** Дамдинова Баира Шойсороновна;**
адрес: Россия, 119992, Москва, ул. Трубецкая, д. 8, стр. 2;
ORCID: 0000-0002-4162-2928;
e-mail: baira_d@mail.ru

Теплюк Наталия Павловна, д-р мед. наук, профессор;
ORCID: 0000-0002-5800-4800;
eLibrary SPIN: 8013-3256;
e-mail: teplyukn@gmail.com

Степанов Михаил Александрович, канд. мед. наук, доцент;
ORCID: 0000-0002-1872-9487;
eLibrary SPIN: 6524-5665;
e-mail: Doctor.stepanov@gmail.com

Stepan V. Toshchakov, Cand. Sci. (Biol.);
ORCID: 0000-0001-7549-3450;
eLibrary SPIN: 8994-5224;
e-mail: stepan.toshchakov@gmail.com

Sergey A. Noskov;
ORCID: 0009-0006-1578-1382;
e-mail: sergey.noskov.2001@icloud.com

Tutubalina Nina Alekseevna;
ORCID: 0009-0004-7016-3670;
e-mail: nina.tutubalina@gmail.com

* Corresponding author / Автор, ответственный за переписку

Тощаков Степан Владимирович, канд. биол. наук;
ORCID: 0000-0001-7549-3450;
eLibrary SPIN: 8994-5224;
e-mail: stepan.toshchakov@gmail.com

Носков Сергей Александрович;
ORCID: 0009-0006-1578-1382;
e-mail: sergey.noskov.2001@icloud.com

Тутубалина Нина Алексеевна;
ORCID: 0009-0004-7016-3670;
e-mail: nina.tutubalina@gmail.com