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Peculiarities of the algorithm of diagnostics of oral mucosa pathology in patients with Crohn's disease and nonspecific ulcerative colitis

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Abstract

INTRODUCTION. The manifestations of Crohn's disease (CD) and ulcerative colitis (UC) in the oral cavity include both nonspecific lesions and specific lesions directly associated with intestinal inflammation. Oral lesions that remain undiagnosed may subsequently be difficult to manage with therapeutic and preventive measures.

AIM. To evaluate the developed diagnostic algorithm for oral mucosal pathology in patients with CD and UC.

MATERIALS AND METHODS. The comprehensive clinical and dental examination included an assessment of complaints, medical history, findings from an objective examination, and laboratory investigations.

RESULTS. This retrospective, multicenter study included young adults with CD and UC who were under regular medical supervision in gastroenterology departments and adhered to general treatment protocols. Clinical manifestations of lip vermilion pathology were observed in 51.43% and 42.85% of patients with CD and UC, respectively ($p < 0.01$), including glossodynia in 31.43% ($p < 0.01$) and 17.15% ($p < 0.05$) of cases. The main complaints of patients with diagnosed oral mucosal pathology were unpleasant sensations in the form of soreness and pain when consuming irritant foods in 100% and 65.71% of cases, respectively; discomfort during speech in 31.43% and 25.71% of cases; and dry mouth in 51.43% and 25.71% of cases. Burning sensation in the oral cavity was reported in 31.43% and 17.15% of patients.

CONCLUSIONS. The correlation between clinical manifestations of oral mucosal pathology and laboratory findings necessitates biochemical monitoring of reduced vitamin B6 and B12 levels in the blood. Deficiency of these vitamins was observed in 42.9% and 28.57% of patients with CD and in 34.4% and 20.0% of patients with UC, justifying the diagnosis of desquamative glossitis (KACD = 0.73 and KAUC = 0.64). The diagnosis of fissured tongue was established in 42.9% and 28.57% of CD patients and in 14.3% and 8.6% of UC patients (KACD = 1.0, KAUC = 0.64). In CD patients in remission with vitamin B12 deficiency, the relative risks for the development of aphthous stomatitis, fissured tongue, and burning mouth syndrome with glossodynia were OR = 7.1 (CI: 1.2–41.0), OR = 11.5 (CI: 1.7–77.2), and OR = 29.3 (CI: 4.1–200.0), respectively. In the same group, vitamin B6 deficiency increased the risk of fissured tongue (OR = 12.7, CI: 1.3–121.4) and burning mouth syndrome with glossodynia (OR = 13.5, CI: 2.3–80.8). In UC patients, deficiencies in vitamin B12 and B6 were criteria for the development of recurrent aphthous stomatitis (OR = 19.2, CI: 1.9–196.5 and OR = 9.2, CI: 1.4–59.6, respectively), fissured tongue (OR = 13.5, CI: 1.6–115.9 and OR = 9.8, CI: 1.2–77.7, respectively), and burning mouth syndrome with glossodynia (OR = 8.7, CI: 1.02–63.8 and OR = 17.3, CI: 2.2–138.2, respectively). Low hemoglobin levels in CD patients increased the risk of geographic glossitis (OR = 4.9, CI: 1.01–29.4) and the manifestation of burning mouth syndrome with glossodynia (OR = 6.0, CI: 1.2–29.7). Interdisciplinary collaboration between dentists, gastroenterologists, general practitioners, and neurologists is essential for the early diagnosis of lip vermilion and oral mucosal pathology in patients with CD and UC manifestations.

Keywords: diagnosis, aphthous stomatitis, glossitis, burning mouth syndrome, Crohn's disease, ulcerative colitis

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Особенности алгоритма диагностики патологии слизистой оболочки рта у пациентов с болезнью Крона и неспецифическими язвенным колитом

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Резюме

ВВЕДЕНИЕ. Проявления болезни Крона (БК) и неспецифического язвенного колита (НЯК) в полости рта включают неспецифические поражения и специфические поражения, непосредственно связанные с воспалением кишечника. Поражения в полости рта, которые могут быть не диагностированы в дальнейшем трудно поддаются лечебно-профилактическим мероприятиям.

ЦЕЛЬ ИССЛЕДОВАНИЯ. Оценка разработанного алгоритма при диагностике патологии слизистой оболочки рта у пациентов с БК и НЯК.

МАТЕРИАЛЫ И МЕТОДЫ. Комплекс клинико-стоматологического обследования включал анализ жалоб, анамнеза, данных обьективного обследования, лабораторного исследования.

РЕЗУЛЬТАТ. В это ретроспективное трехцентровое исследование были включены лица молодого возраста с БК и НЯК, которые находились на диспансерном наблюдении в гастроэнтерологических отделениях и соблюдали требования общего лечения. При БК и НЯК клинические проявления патологии красной каймы губ выявлены у 51,43% и 42,85% лиц ($p < 0,01$), в том числе глоссодинии в 31,43% ($p < 0,01$) и 17,15% ($p < 0,05$) случаев. Основными жалобами пациентов при выявленной патологии СОР были неприятные ощущения в виде ссаднения и болезненности при приеме, раздражающей пиши в 100% и 65,71% случаев, при разговоре в 31,43% и 25,71% случаев, на наличие сухости в полости рта в 51,43% и 25,71% случаев. Симптом жжения полости рта выявлен у 31,43% и 17,15% пациентов.

ВЫВОДЫ. Взаимосвязь клинических проявлений патологии слизистой оболочки рта с лабораторными показателями предусматривает биохимический мониторинг в крови сниженного уровня витамина В6 и В12, что соответственно в 42,9%, 28,57% случаев при болезни Крона, в 34,4%, 20,0% случаев при неспецифическом язвенном колите обосновывает постановку диагноза десквамативный глоссит ($КА_{БК} = 0,73$ и $КА_{НЯК} = 0,64$), в 42,9%, 28,57% случаях при болезни Крона БК и в 14,3%, 8,6% случаях неспецифического язвенного колита диагностику складчатого языка ($КА_{БК} = 1,0$, $КА_{НЯК} = 0,64$). У пациентов с БК в стадии ремиссии при наличии дефицита витамина В12 в крови относительные шансы и доверительных интервалов развития афтозного стоматита составляют с OR = 7,1 (CI: 1,2–41,0), складчатого языка с OR = 11,5 (CI: 1,7–77,2), синдрома жжения полости рта, глоссодинии с OR = 29,3 (CI: 4,1–200,0). При дефиците В6 у этих же больных возрастает риск складчатого языка с OR = 12,7 (CI: 1,3–121,4) и синдрома жжения полости рта, глоссодинии с OR = 13,5 (CI: 2,3–80,8). У больных с НЯК при наличии дефицита витаминов В12 и В6 в крови является критерием для развития рецидивирующего афтозного стоматита (OR = 19,2 (CI: 1,9–196,5) и OR = 9,2 (CI: 1,4–59,6) соответственно, складчатого языка (OR = 13,5 (CI: 1,6–115,9) и OR = 9,8 (CI: 1,2–77,7), соответственно, синдрома жжения полости рта, глоссодинии (OR = 8,7 (CI: 1,02–63,8) и OR = 17,3 (CI: 2,2–138,2), соответственно). Низкий уровень гемоглобина у пациентов с БК повышал риск клинического течения географического глоссита (OR = 4,9 (CI: 1,01–29,4)) и проявлений синдрома жжения полости рта и глоссодинии (OR = 6,0 (CI: 1,2–29,7).

ЗАКЛЮЧЕНИЕ. Междисциплинарное сотрудничество между стоматологами, гастроэнтерологами, терапевтами, неврологами является критерием ранней диагностики патологии красной каймы губ и слизистой оболочки рта у пациентов с проявлениями БК и НЯК.

Ключевые слова: диагностика, афтозный стоматит, глоссит, синдром жжения полости рта, болезнь Крона, неспецифический язвенный колит

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INTRODUCTION

Inflammatory bowel diseases (IBD) primarily include ulcerative colitis (UC) and Crohn's disease (CD). Both conditions have significant social relevance, as the primary cohort of patients predominantly consists of young, working-age individuals who fall into the category of "chronically ill" and require frequent hospitalizations [1].

According to data obtained from 78 regions of Russia, inflammatory bowel diseases (IBD) have been diagnosed in 3,827 patients, including 2,358 cases of ulcerative colitis (UC) and 1,469 cases of Crohn's disease (CD) [1]. The global number of IBD patients exceeds 4.9 million. In Europe, the incidence of CD ranges between 0.4 and 22.8 per 100,000 people per year, while the incidence of UC varies between 2.4 and 44.0 per 100,000 people per year [2; 3].

From an epidemiological perspective, CD affects men and women equally. The age of disease onset follows a bimodal distribution, with a peak between 20 and 40 years and a second peak between 50 and 60 years. The incidence and prevalence of the disease have significantly increased worldwide [4].

The presence of oral manifestations that precede or follow the intestinal symptoms of Crohn's disease (CD) and ulcerative colitis (UC) should be a matter of serious attention for dentists, gastroenterologists, and general practitioners to ensure early diagnosis [5; 6].

Oral mucosal pathology associated with the clinical course of CD and UC may be observed in more than 60% of patients and is more frequently found in males and those diagnosed with inflammatory bowel disease (IBD) at a younger age [7; 8]. In this patient category, nonspecific oral manifestations such as aphthous stomatitis and glossitis [9; 10], as well as burning mouth syndrome, may appear several years before the onset of systemic symptoms [10].

Extraintestinal orofacial manifestations often go unnoticed during a clinical examination by a gastroenterologist, leading to suboptimal management of this patient group. On average, 50% of practicing gastroenterologists and general practitioners experience difficulties in the early diagnosis of oral mucosal lesions compared to dentists [11].

According to the literature, extraintestinal manifestations of Crohn's disease (CD) and ulcerative colitis (UC) are directly associated not only with changes in dental and general health status but also with alterations in blood parameters [12].

The presence of oral mucosal lesions should raise suspicion of inflammatory bowel disease (IBD) not only in its active stage but also during remission, even in the absence of pronounced or any gastrointestinal symptoms. Since oral lesions may precede the onset of CD and UC, early diagnosis requires close collaboration between dental specialists and gastroenterologists [13], which underlines the relevance and objective of our study.

AIM

The aim of the study was to develop and implement a diagnostic algorithm for detecting pathology of the lip vermilion and oral mucosa in patients with manifestations of Crohn's disease and ulcerative colitis in clinical practice.

MATERIALS AND METHODS

From 2020 to 2022, a comprehensive clinical and dental non-randomized, open-label, multicenter study was conducted at GBUZ RB City Clinical Hospital No. 21 in Ufa, the BSMU Clinic, and the Republican Clinical Hospital (RCH). The study included a retrospective analysis of medical records of 70 patients diagnosed with chronic inflammatory bowel diseases (CIBD). Based on the results, two clinical groups were formed:

1. The first group included 35 patients with Crohn's disease (CD), with a mean age of 37.5 ± 1.6 years.

2. The second group consisted of 35 patients with ulcerative colitis (UC), with a mean age of 42.2 ± 1.8 years.

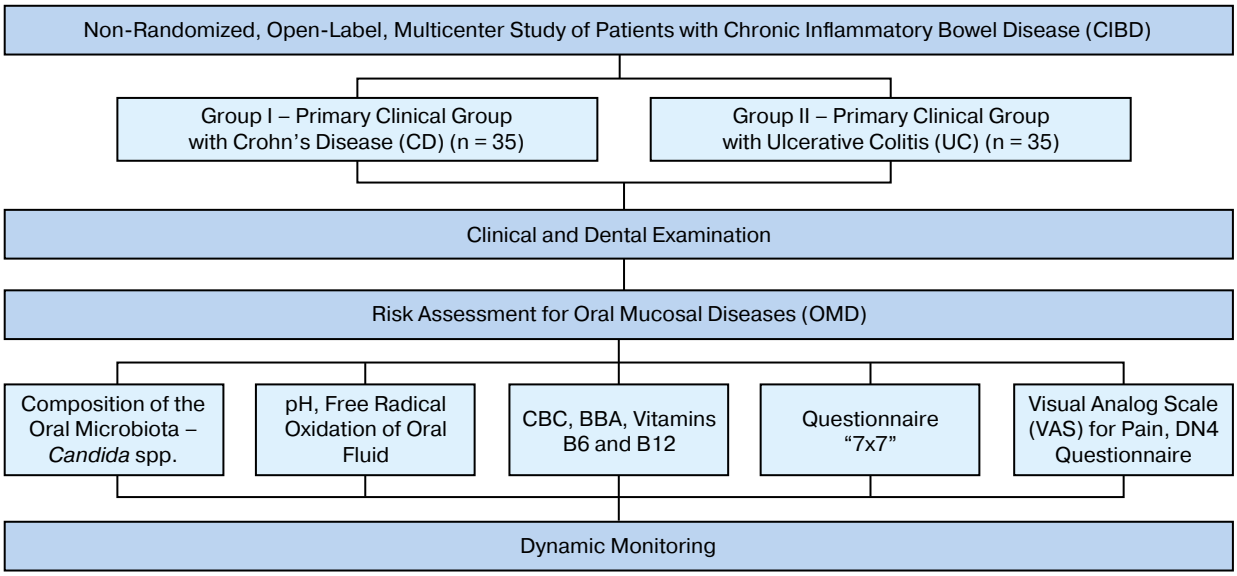

Fig. 1. Study design

Рис. 1. Дизайн исследования

All participants with clinical manifestations of CIBD underwent treatment at GBUZ RB City Clinical Hospital No. 21, the BSMU Clinic, and RCH in Ufa. Based on medical record data, clinical features, laboratory parameters, and endoscopic findings, we identified risk factors, the nature of the clinical course, remission duration, and the frequency of relapses in CD and UC.

The design of the comprehensive clinical and dental examination is presented in Fig. 1.

To describe the characteristics, medians and interquartile ranges were used for quantitative variables, while relative frequencies were used for categorical variables. Group comparisons were performed using the chi-square test for categorical variables and the Mann-Whitney test for quantitative variables. Differences were considered statistically significant at $p < 0.05$.

To assess the association between clinical manifestations of oral mucosal pathology and laboratory parameters in patients with Crohn's disease (CD) and ulcerative colitis (UC), association coefficients were calculated. Since the significance of association coefficients cannot be tested using standard hypothesis testing procedures, an association was considered present when the coefficient exceeded 0.5.

To evaluate the risk of oral mucosal diseases in patient groups, odds ratios (OR) and confidence intervals (CI) were calculated. For better visualization of odds ratio, a forest plot was constructed. All statistical analyses were performed using the R programming language.

RESULTS

In our study, anemia was observed in 31.4% ($n = 70$) of patients. Although the prevalence of anemia was 1.2 times lower in Crohn's disease (CD) (28.57%) compared to ulcerative colitis (UC) (34.29%), these differences were not statistically significant ($p = 0.607$). The median hemoglobin concentration in IBD patients was 118.5 g/L, with 120 g/L in CD and 117 g/L in UC ($p = 0.299$, Table 1).

A comprehensive general therapeutic blood analysis revealed that patients with inflammatory bowel disease (IBD) exhibited deficiencies in hemoglobin, iron, vitamin B12, and vitamin B6, while ferritin levels were at the lower limit of the normal range (Table 1). Comparative analysis demonstrated that vitamin B12 and B6 deficiencies were significantly more pronounced in CD patients than in UC patients ($p < 0.001$).

A comprehensive clinical and dental examination of patients with IBD allowed us to determine the prevalence of oral mucosal pathology in patients with CD and UC. However, no significant differences in their distribution between the patient groups were identified ($p > 0.1$, Table 2).

The calculation of association coefficients to assess the relationship between clinical manifestations of oral mucosal pathology and laboratory parameters in patients with Crohn's disease (CD) and ulcerative colitis (UC) demonstrated a significant impact of vitamin B6 and B12 deficiencies on the occurrence of aphthous stomatitis. This association was found to be stronger in UC patients than in those with CD.

Additionally, deficiencies in vitamins B6 and B12 were linked to the frequency of burning mouth syndrome and fissured tongue, with similar associations observed in both CD and UC patients.

Low hemoglobin levels (below normal) contributed to the development of recurrent aphthous stomatitis, geographic glossitis, and burning mouth syndrome, but only in CD patients.

Table 3 presents the cross-tabulated frequencies for CD and UC patients with hemoglobin, vitamin B6, and vitamin B12 levels below normal (considering sex-specific reference values) and the corresponding prevalence of oral mucosal diseases in these groups.

Table 1. Median values of the comprehensive general therapeutic blood analysis in patients with Crohn's disease (CD) and ulcerative colitis (UC) (median [interquartile range])

Таблица 1. Медианные показатели развернутого общетерапевтического анализа крови у пациентов с БК и НЯК (медиана (межквартильный размах))

Blood test parameters	Group I – Primary clinical group with Crohn's disease (CD), ICD-10 code: K50 ($n = 35$)	Group II – Primary clinical group with ulcerative colitis (UC), ICD-10 code: K51 ($n = 35$)
	***Z*-statistic#, *p*-value**	
Hemoglobin, g/L Men: 130–160 g/L, Women: 120–140 g/L	120 (113–132)	117 (103.0–135.5)
	$Z = 1.04$; $p = 0.299$	
Serum iron, μmol/L Men: 9–31 μmol/L, Women: 9–31 μmol/L	9.9 (5.7–15.6)	11 (4.8–18.4)
	$Z = 0.07$; $p = 0.943$	
Vitamin B6 Normal range: 20–125 ng/mL	55 (29–70)	122 (96–140)
	$Z = 9.60^{***}$; $p < 0.001$	
Vitamin B12, ng/mL Normal range: 87–883 ng/mL	274.5 (241–313)	417 (389–496)
	$Z = 9.03^{***}$; $p < 0.001$	
Leukocytes Normal range: $4–9 \times 10^9$/L	6.7 (5.3–8.0)	7.3 (6.1–8.4)
	$Z = 1.33$; $p = 0.183$	
Erythrocytes Men: $4–5 \times 10^{12}$/L Women: $3.9–4.7 \times 10^{12}$/L	4.5 (4.2–4.9)	4.5 (4.1–4.9)
	$Z = 0.27$; $p = 0.786$	
Erythrocyte Sedimentation Rate (ESR) Men: 2–10 mm/h Women: 2–15 mm/h	14 (7–16)	17 (10–32)
	$Z = 2.27^{*}$; $p = 0.024$	
Serum Ferritin, μg/L Men: 30.00–400.00 μg/L Women: 13.00–150.00 μg/L	43.5 (14–104)	41.5 (19–138)
	$Z = 0.92$; $p = 0.350$	

Note: # According to the Mann-Whitney test; *, *** Statistically significant differences at the level of $p < 0.05$ and $p < 0.001$, respectively.

Примечания: # Согласно критерию Мана-Уитни; *, *** Статистически значимые различия при уровне $p < 0,05$ и $p < 0,001$, соответственно.

Table 2. The prevalence of oral mucosal pathology in patients with Crohn's disease (CD) and ulcerative colitis (UC)

Таблица 2. Частота встречаемости патологии слизистой оболочки рта у пациентов с БК и НЯК

Oral Mucosal Pathology	Group I – Primary Clinical Group with Crohn's Disease (CD), ICD-10 Code: K50 (*n* = 35)	Group II – Primary Clinical Group with Ulcerative Colitis (UC), ICD-10 Code: K51 (*n* = 35)	χ^2-statistic#	*p*-value
Recurrent aphthous stomatitis (ICD-10: K12.0)	17 (48.5%)	11 (31.4%)	2.143	0.144
Geographic glossitis (ICD-10: K14.1) (Desquamative or migratory glossitis)	15 (42.9%)	11 (31.4%)	0.979	0.323
Fissured tongue (Scrotal, furrowed glossitis) (ICD-10: K14.5)	7 (20.0%)	5 (14.3%)	0.402	0.526
Burning mouth syndrome, glossodynia (ICD-10: K14.6)	11 (31.4%)	6 (17.2%)	1.942	0.164

Note: #The chi-square (χ^2) test.

Примечания: #Согласно χ^2-критерию.

Table 3. Association between clinical manifestations of oral mucosal pathology and laboratory parameters in patients with Crohn's disease (CD) and ulcerative colitis (UC), association coefficients

Таблица 3. Взаимосвязь клинических проявлений патологии слизистой оболочки рта с лабораторными показателями у пациентов с БК и НЯК, коэффициенты ассоциации

Association of Disease Symptoms with Oral Mucosal Pathology (OMP)	Group I – Primary Clinical Group with Crohn's Disease (CD), ICD-10 Code: K50 (*n* = 35)		Group II – Primary Clinical Group with Ulcerative Colitis (UC), ICD-10 Code: K51 (*n* = 35)	
	абс.	%	абс.	%
	Association Coefficients			
Low Hemoglobin Levels / Recurrent Aphthous Stomatitis (ICD-10: K12.0)	10/7	28.57/41.17	16/5	45.71/45.45
	KA_{CD} = 0.56		KA_{UC} = 0.07	
Lower Border of Vitamin B12 / Recurrent Aphthous Stomatitis (ICD-10: K12.0)	10/8	28.57/47.06	6/5	17.14/45.45
	KA_{CD} = 0.75		KA_{UC} = 0.9	
Lower Border of Vitamin B6 / Recurrent Aphthous Stomatitis (ICD-10: K12.0)	15/10	42.86/58.8	7/5	20.0/45.45
	KA_{CD} = 0.58		KA_{UC} = 0.8	
Low Hemoglobin Levels / Geographic Glossitis (ICD-10: K14.1) (Desquamative or Migratory Glossitis)	10/7	28.57/46.7	16/6	45.71/54.55
	KA_{CD} = 0.66		KA_{UC} = 0.25	
Lower Border of Vitamin B12 / Geographic Glossitis (ICD-10: K14.1) (Desquamative or Migratory Glossitis)	10/6	28.57/40.0	6/2	17.14/18.18
	KA_{CD} = 0.45		$KA_{UC}C$ = 0.05	
Lower Border of Vitamin B6 / Geographic Glossitis (ICD-10: K14.1) (Desquamative or Migratory Glossitis)	15/8	42.86/5.33	7/3	20.0/27.27
	KA_{CD} = 0.36		KA_{UC} = 0.3	
Low Hemoglobin Levels / Fissured Tongue (Scrotal, Furrowed Glossitis) (ICD-10: K14.5)	10/4	28.57/57.14	16/4	45.71/80.0
	KA_{CD} = 0.66		KA_{UC} = 0.71	
Lower Border of Vitamin B12 / Fissured Tongue (Scrotal, Furrowed Glossitis) (ICD-10: K14.5)	10/5	28.57/17.14	6/3	17.14/60.0
	KA_{CD} = 0.84		KA_{UC} = 0.86	
Lower Border of Vitamin B6 / Fissured Tongue (Scrotal, Furrowed Glossitis) (ICD-10: K14.5)	15/6	42.86/85.71	7/3	20.0/60.0
	KA_{CD} = 0.86		KA_{UC} = 0.81	
Low Hemoglobin Levels / Burning Mouth Syndrome, Glossodynia (ICD-10: K14.6)	10/6	28.57/54.55	16/2	45.71/33.33
	KA_{CD} = 0.71		KA_{UC} = 0.3	
Lower Border of Vitamin B12 / Burning Mouth Syndrome, Glossodynia (ICD-10: K14.6)	10/8	42.86/72.73	6/3	17.14/50.0
	KA_{CD} = 0.93		KA_{UC} = 0.79	
Lower Border of Vitamin B6 / Burning Mouth Syndrome, Glossodynia (ICD-10: K14.6)	15/9	42.86/81.82	7/4	20.0/66.66
	KA_{CD} = 0.86		KA_{UC} = 0.89	

Note: KA_{CD} – Association coefficient between characteristics for patients with Crohn's disease (CD); KA_{UC} – Association coefficient between characteristics for patients with ulcerative colitis (UC).

Примечания: КАБК – коэффициент ассоциации между признаками для пациентов с БК, КАНЯК – коэффициент ассоциации между признаками для пациентов с НЯК.

Additionally, to assess the extent to which hemoglobin, vitamin B6, and vitamin B12 deficiencies contribute to the development of oral mucosal pathologies, odds ratios (OR) were calculated, along with the lower and upper confidence interval (Lower CI and Upper CI) boundaries, separately for Crohn's disease (CD) and ulcerative colitis (UC).

Based on these calculations, forest plots were constructed (Fig. 2–7).

The calculation of odds ratios (OR) and confidence intervals (CI) demonstrated that in patients with Crohn's disease (CD), vitamin B12 deficiency increased the likelihood of developing recurrent aphthous stomatitis (OR = 7.1, CI: 1.2–41.0), fissured tongue (OR = 11.5, CI: 1.7–77.2), and burning mouth syndrome with glossodynia (OR = 29.3, CI: 4.1–200.0). In the same group, vitamin B6 deficiency was associated with an increased risk of fissured tongue (OR = 12.7, CI: 1.3–121.4) and burning mouth syndrome with glossodynia (OR = 13.5, CI: 2.3–80.8).

Vitamin B12 and B6 deficiencies also contributed to the development of oral mucosal diseases in patients with ulcerative colitis (UC): recurrent aphthous stomatitis (OR = 19.2, CI: 1.9–196.5 and OR = 9.2, CI: 1.4–59.6, respectively), fissured tongue (OR = 13.5, CI: 1.6–115.9 and OR = 9.8, CI: 1.2–77.7, respectively), and burning mouth syndrome with glossodynia (OR = 8.7, CI: 1.02–63.8 and OR = 17.3, CI: 2.2–138.2, respectively).

Furthermore, low hemoglobin levels, based on our study findings, increased the risk of geographic glossitis (OR = 4.9, CI: 1.01–29.4) and burning mouth syndrome with glossodynia (OR = 6.0, CI: 1.2–29.7), but only in CD patients.

OMD in CD and decreased Hb	Odds Ratio	Lower CI	Upper CI
Recurrent aphthous stomatitis	3.50	0.73	16.85
Geographic glossitis	4.96	1.01	24.37
Plicated tongue	4.89	0.85	20.08
Burning mouth syndrome, glossodynia	6.00	1.21	29.73

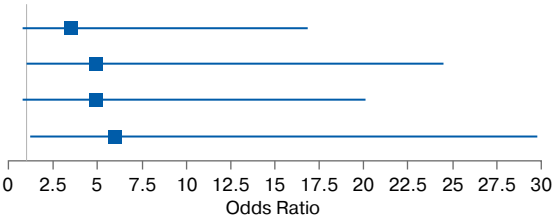

Fig. 2. Forest-plot Odds Ratio and CI for Oral mucosal diseases (OMD) in Crohn's disease (CD) and decreased Hb

Рис. 2. Лесной график (Forest plot) отношения шансов (OR) и доверительного интервала (CI) для заболеваний слизистой оболочки рта (ОМЗ) при болезни Крона (БК) и снижении уровня гемоглобина (Hb)

OMD in NSUC and decreased Hb	Odds Ratio	Lower CI	Upper CI
Recurrent aphthous stomatitis	0.99	0.24	4.08
Geographic glossitis	1.68	0.39	7.08
Plicated tongue	6.00	0.59	60.44
Burning mouth syndrome, glossodynia	0.54	0.08	3.39

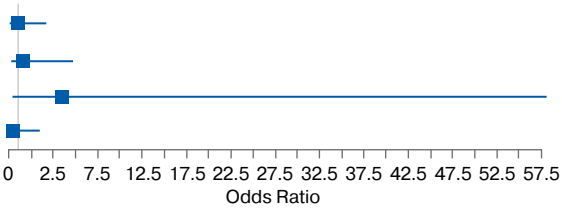

Fig. 3. Forest-plot Odds Ratio and CI for Oral mucosal diseases (OMD) in non-specific ulcerative colitis (NSUC) and decreased Hb

Рис. 3. Лесной график (Forest plot) отношения шансов (OR) и доверительного интервала (CI) для заболеваний слизистой оболочки рта (ОМЗ) при неспецифическом язвенном колите (НЯК) и снижении уровня гемоглобина (Hb)

OMD in CD and B12 deficiency	Odds Ratio	Lower CI	Upper CI
Recurrent aphthous stomatitis	7.11	1.23	40.98
Geographic glossitis	2.67	0.59	12.02
Plicated tongue	11.50	1.71	77.18
Burning mouth syndrome, glossodynia	29.33	4.12	200.02

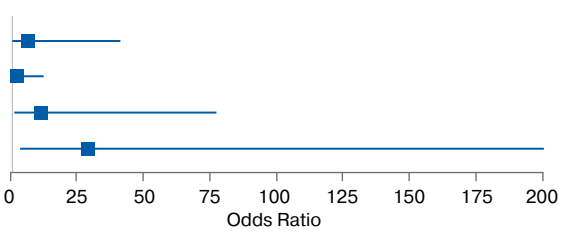

Fig. 4. Forest-plot Odds Ratio and CI for Oral mucosal diseases (OMD) in Crohn's disease (CD) and B12 deficiency

Рис. 4. Лесной график (Forest plot) отношения шансов (OR) и доверительного интервала (CI) для заболеваний слизистой оболочки рта (ОМЗ) при болезни Крона (БК) и дефиците витамина B12

OMD in NCUC and B12 deficiency	Odds Ratio	Lower CI	Upper CI
Recurrent aphthous stomatitis	19.16	1.87	196.50
Geographic glossitis	1.11	0.17	7.22
Plicated tongue	13.50	1.571	115.94
Burning mouth syndrome, glossodynia	8.67	1.02	63.84

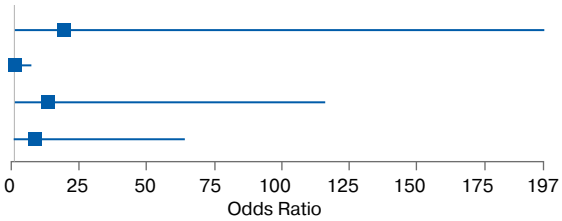

Fig. 5. Forest-plot Odds Ratio and CI for Oral mucosal diseases (OMD) in non-specific ulcerative colitis (NSUC) and B 12 deficiency

Рис. 5. Лесной график (Forest plot) отношения шансов (OR) и доверительного интервала (CI) для заболеваний слизистой оболочки рта (ОМЗ) при неспецифическом язвенном колите (НЯК) и дефиците витамина В12

OMD in CD and B6 deficiency	Odds Ratio	Lower CI	Upper CI
Recurrent aphthous stomatitis	3.71	0.90	15.26
Geographic glossitis	2.12	0.54	8.43
Plicated tongue	12.67	1.32	121.43
Burning mouth syndrome, glossodynia	13.50	2.26	80.79

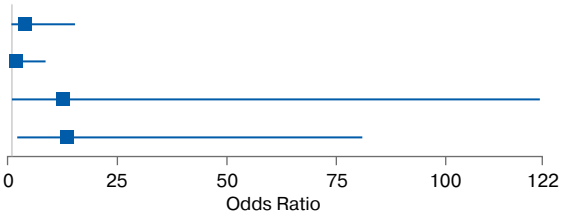

Fig. 6. Forest-plot Odds Ratio and CI for Oral mucosal diseases (OMD) in Crohn's disease (CD) and B 6 deficiency

Рис. 6. Лесной график (Forest plot) отношения шансов (OR) и доверительного интервала (CI) для заболеваний слизистой оболочки рта (ОМЗ) при болезни Крона (БК) и дефиците витамина В6

OMD in NSUC and B6 deficiency	Odds Ratio	Lower CI	Upper CI
Recurrent aphthous stomatitis	9.17	1.41	59.59
Geographic glossitis	1.88	0.34	10.33
Plicated tongue	9.75	1.23	77.73
Burning mouth syndrome, glossodynia	17.33	2.17	138.18

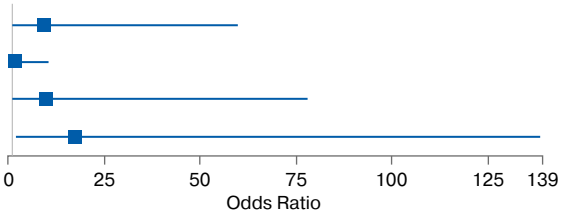

Fig. 7. Forest-plot Odds Ratio and CI for Oral mucosal diseases (OMD) in non-specific ulcerative colitis (NSUC) and B 6 deficiency

Рис. 7. Лесной график (Forest plot) отношения шансов (OR) и доверительного интервала (CI) для заболеваний слизистой оболочки рта (ОМЗ) при неспецифическом язвенном колите (НЯК) и дефиците витамина В6

DISCUSSION

The European Crohn's and Colitis Organization (ECCO) classifies anemia in patients with Crohn's disease (CD) and ulcerative colitis (UC) into iron deficiency anemia (IDA), anemia of chronic disease (ACD), and anemia associated with vitamin B12 or folic acid deficiency [12]. Additionally, a previous study [10] reported that oral lesions occur with nearly the same frequency regardless of the type of inflammatory bowel disease (IBD), which is consistent with our findings.

According to data from a retrospective study of 257 patients with CD and 208 patients with UC who had anemia, the mean hemoglobin levels in a complete blood count (CBC) were 12.1 g/dL for CD and 12.5 g/dL for UC [14], which aligns with our study results. The prevalence of anemia was higher in CD (62.1%) compared to UC (55.7%) (p = 0.04) [15], whereas our study did not identify a significant difference (p = 0.138).

Extraintestinal manifestations (EIMs) of IBD are diverse and may be secondary to the disease, a reaction to IBD, associated with it, or a consequence of nutrient deficiencies. The most common vitamin and nutrient deficiencies in IBD patients include iron, vitamin B6, and vitamin B12, which contribute to the clinical course of glossitis and burning mouth syndrome [16; 17].

Recurrent aphthous stomatitis (RAS) may arise as a manifestation of IBD and is considered an extraintestinal feature [18; 19]. However, glossitis may not always be a direct part of IBD but rather a consequence of

nutritional deficiencies induced by the disease [20], which is consistent with our study findings.

Various studies have identified several oral manifestations associated with ulcerative colitis (UC). These include recurrent aphthous ulcers (RAU), atrophic glossitis (AG), which affects taste perception, burning mouth syndrome (BMS), and angular cheilitis (AC). These manifestations can sometimes serve as early indicators of the clinical course of Crohn's disease (CD) and UC and are valuable for monitoring patients' health status [9; 21], further confirming the association between oral mucosal pathology and IBD found in our study.

The main symptoms in patients with CD and UC include chronic diarrhea and secondary anemia, while extraintestinal oral manifestations are observed in this population, with a prevalence ranging from 16.7% to 40% [22], which is consistent with our findings.

The obtained data on the relationship between the clinical course of oral mucosal pathology (including aphthous stomatitis, glossitis, and burning mouth syndrome) in CD and UC patients during remission align with the results of recent clinical studies.

CONCLUSIONS

The association between clinical manifestations of oral mucosal pathology and laboratory parameters necessitates biochemical monitoring of blood levels of vitamin B6 and B12. A deficiency of these vitamins was observed in 42.9% and 28.57% of patients with Crohn's disease (CD) and in 34.4% and 20.0% of patients with ulcerative colitis (UC), which justifies the diagnosis of desquamative glossitis ($KA_{CD} = 0.73$, $KA_{UC} = 0.64$). Additionally, fissured tongue was diagnosed in 42.9% and 28.57% of CD patients and in 14.3% and 8.6% of UC patients ($KA_{CD} = 1.0$, $KA_{UC} = 0.64$).

In CD patients in remission, the presence of vitamin B12 deficiency increased the odds ratio (OR) for the development of:

– aphthous stomatitis (OR = 7.1, CI: 1.2–41.0);

– fissured tongue (OR = 11.5, CI: 1.7–77.2);

– burning mouth syndrome and glossodynia (OR = 29.3, CI: 4.1–200.0).

In the same group, vitamin B6 deficiency significantly increased the risk of:

– fissured tongue (OR = 12.7, CI: 1.3–121.4);

– burning mouth syndrome and glossodynia (OR = 13.5, CI: 2.3–80.8).

In UC patients, vitamin B12 and B6 deficiencies were critical factors for the development of:

– recurrent aphthous stomatitis (OR = 19.2, CI: 1.9–196.5 and OR = 9.2, CI: 1.4–59.6, respectively);

– fissured tongue (OR = 13.5, CI: 1.6–115.9 and OR = 9.8, CI: 1.2–77.7, respectively);

– burning mouth syndrome and glossodynia (OR = 8.7, CI: 1.02–63.8 and OR = 17.3, CI: 2.2–138.2, respectively).

Low hemoglobin levels in CD patients increased the risk of:

– geographic glossitis (OR = 4.9, CI: 1.01–29.4);

– burning mouth syndrome and glossodynia (OR = 6.0, CI: 1.2–29.7).

Thus, the chronic course of CD and UC in remission serves as a criterion for developing a diagnostic algorithm for oral mucosal pathology in IBD patients, with the goal of integrating it into clinical practice.

The results of this study confirm that extraintestinal oral manifestations can precede gastrointestinal symptoms in CD and UC. Dentists, during clinical examinations, can identify these extraintestinal manifestations and contribute to the early diagnosis of IBD.

REFERENCES / СПИСОК ЛИТЕРАТУРЫ

1. Belousova E.A., Shelygin Yu.A., Achkasov S.I., Khatkov I.E., Bakulin I.G., Skalinskaya M.I. et al. Clinical and Demographic Features and Treatment Approaches for Inflammatory Bowel Diseases (Crohn's Disease, Ulcerative Colitis) in the Russia. The Primery Results of the Analysis of the National Register. *Koloproktologia*. 2023;22(1):65–82. https://doi.org/10.33878/2073-7556-2023-22-1-65-82
Белоусова Е.А., Шелыгин Ю.А., Ачкасов С.И., Хатьков И.Е., Бакулин И.Г., Скалинская М.И и др. Клинико-демографические характеристики и лечебные подходы у пациентов с воспалительными заболеваниями кишечника (болезнь Крона, язвенный колит) в РФ. Первые результаты анализа национального Регистра. *Колопроктология*. 2023;22(1):65–82. https://doi.org/10.33878/2073-7556-2023-22-1-65-82
2. Wang R., Li Z., Liu S., Zhang D. Global, regional and national burden of inflammatory bowel disease in 204 countries and territories from 1990 to 2019: a systematic analysis based on the Global Burden of Disease Study 2019. *BMJ Open*. 2023;13(3):e065186. https://doi.org/10.1136/bmjopen-2022-065186
3. Dou Z., Zheng H., Shi Y., Li Y., Jia J. Analysis of global prevalence, DALY and trends of inflammatory bowel disease and their correlations with sociodemographic index: Data from 1990 to 2019. *Autoimmun Rev*. 2024;23(11):103655. https://doi.org/10.1016/j.autrev.2024.103655
4. Pecci-Lloret M.P., Ramirez-Santisteban E., Hergueta-Castillo A., Guerrero-Gironés J., Oñate-Sánchez R.E. Oral Manifestations of Crohn's Disease: A Systematic Review. *J Clin Med*. 2023;12(20):6450. https://doi.org/10.3390/jcm12206450
5. Joshi S., Moore A., Mawdsley J., Carey B. Oral manifestations of inflammatory bowel disease: a guide to examination. *Frontline Gastroenterol*. 2024;15:328–335. https://doi.org/10.1136/flgastro-2023-102619
6. Alrashdan M.S., Safadi R.A. Crohn's disease initially presenting with oral manifestations and managed with ustekinumab: A case report. *Spec Care Dentist*. 2021;41(5):634–638. https://doi.org/10.1111/scd.12598
7. Tan C.X., Brand H.S., de Boer N.K., Forouzanfar T. Gastrointestinal diseases and their oro-dental manifestations: Part 1: Crohn's disease. *Br Dent J*. 2016;221(12):794–799. https://doi.org/10.1038/sj.bdj.2016.954
8. Fine S., Nee J., Thakuria P., Duff B., Farraye F.A., Shah S.A. Ocular, auricular, and oral manifestations of inflammatory bowel disease. *Dig Dis Sci*. 2017;62(12):3269–3279. https://doi.org/10.1007/s10620-017-4781-x

9. Karakoyun M., Tasci E.K., Sezak M., Yasar B.E., Cetin F. Orofacial crohn's disease: A case report. *J. Pediatr. Res*. 2019;6(4):353–355. https://doi.org/10.4274/jpr.galenos.2019.26213
10. Lauritano D., Boccalari E., Di Stasio D., Della Vella F., Carinci F., Lucchese A., Petruzzi M. Prevalence of oral lesions and correlation with intestinal symptoms of inflammatory bowel disease: A systematic review. *Diagnostics*. 2019;9(3):77. https://doi.org/10.3390/diagnostics9030077
11. Cagir Y., Durak M.B., Simsek C., Yuksel I. Specific Oral Manifestations in Adults with Crohn's Disease. *J Clin Med*. 2024;13(13):3955. https://doi.org/10.3390/jcm13133955
12. Mahadea D., Adamczewska E., Ratajczak A.E., Rychter A.M., Zawada A., Eder P. et al. Iron deficiency anemia in inflammatory bowel diseases – A narrative review. *Nutrients*. 2021;13(11):4008. https://doi.org/10.3390/nu13114008
13. Tan C.X.W., Brand H.S., Qaddour O., van der Bijl P.M.L., De Boer N.K.H., Forouzanfar T., de Visscher J.G.AM. Knowledge and Interdisciplinary Communication of Gastroenterologists and dentists in the Netherlands about gastrointestinal diseases with oral manifestations. *Crohns Colitis 360*. 2022;4(1):otac006. https://doi.org/10.1093/crocol/otac006
14. Bengi G., Keyvan H., Durmaz S.B., Akpınar H. Frequency, types, and treatment of anemia in Turkish patients with inflammatory bowel disease. *World J Gastroenterol*. 2018;24(36):4186–4196. https://doi.org/10.3748/wjg.v24.i36.4186
15. Le T.A., Saha S., Shields B.E. Micronutrient deficiencies in patients with inflammatory bowel disease. *Cutis*. 2024;113(4):159–166. https://doi.org/10.12788/cutis.0993
16. Chiang C.P., Yu-Fong Chang J., Wang Y.P., Wu Y.C., Wu Y.H., Sun A. Anemia, hematinic deficiencies, hyperhomocysteinemia, and serum gastric parietal cell antibody positivity in atrophic glossitis patients with or without microcytosis. *J Formos Med Assoc*. 2019;118(10):1401–1407. https://doi.org/10.1016/j.jfma.2019.06.004
17. Atuğ Ö., Kani H.T., Banzragch M., İmeryüz N., Akın H. Incidence rate of anemia in inflammatory bowel diseases. *Turk J Gastroenterol*. 2016;27(2):143–148. https://doi.org/10.5152/tjg.2016.16011
18. King D., Chandan J.S., Thomas T., Nirantharakumar K., Reulen R.C., Adderley N.J., Trudgill N. The risk of later diagnosis of inflammatory bowel disease in patients with dermatological disorders associated with inflammatory bowel disease. *Inflamm Bowel Dis*. 2021;27(11):1731–1739. https://doi.org/10.1093/ibd/izaa344
19. Saikaly S.K., Saikaly T.S., Saikaly L.E. Recurrent aphthous ulceration: a review of potential causes and novel treatments. *J Dermatolog Treat*. 2018;29(6):542–552. https://doi.org/10.1080/09546634.2017.1422079
20. Alrashdan M.S., Safadi R.A. Crohn's disease initially presenting with oral manifestations and managed with ustekinumab: A case report. *Spec Care Dentist.* 2021;41(5):634–638. https://doi.org/10.1111/scd.12598
21. Li C., Wu Y., Xie Y., Zhang Y., Jiang S., Wang J. et al. Oral manifestations serve as potential signs of ulcerative colitis: A review. *Front Immunol*. 2022;13:1013900. https://doi.org/10.3389/fimmu.2022.1013900
22. Greuter T., Bertoldo F., Rechner R., Straumann A., Biedermann L., Zeitz J. et al. Extraintestinal manifestations of pediatric inflammatory bowel disease: prevalence, presentation, and Anti-TNF treatment. *J Pediatr Gastroenterol Nutr*. 2017;65(2):200–206. https://doi.org/10.1097/MPG.0000000000001455

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