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THE CHARACTERISTICS OF MICROBIAL LANDSCAPE OF THE ORAL CAVITY IN PATIENTS WITH VIRAL HEPATITIS B, VIRAL HEPATITIS C AND HIV INFECTION

Azatyan V.Yu.[1]*, Yessayan L.K.[1], Shmavonyan M.V.[2], Porksheyan K.A.[3]

[1] Department of Therapeutic Stomatology, Dental Clinic No 1, Yerevan State Medical University after M. Heratsi, Yerevan, Armenia
[2] Department of Infectious Diseases, Yerevan State Medical University after M. Heratsi, Yerevan, Armenia
[3] Department of Diagnostic Radiology, Yerevan State Medical University after M. Heratsi, Yerevan, Armenia

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Abstract

Viral hepatitis and human immunodeficiency virus (HIV) remain a major global public health problem. The microbiota plays a key role in maintaining normal homeostasis, morphogenesis, metabolism and immune system function.

The aim of the study was to examine the most frequently detected oral microorganisms in patients with viral hepatitis B, C and HIV-infection.

The main study group included 135 patients (I group with hepatitis B virus n=45, II group with hepatitis C virus n=45, III group HIV-infection n=45, IV group control group n=45) with oral mucosal lesions in the age range of 18-67 years. The control group involved 45 patients without hepatitis B virus, hepatitis C virus and HIV-infection with oral mucosal lesions, their age fluctuated from 20 to 69.

We have studied the features of the formation of pathological biotopes in the oral cavity of patients with viral hepatitis B, C and HIV. The results of the microbiological examination of the oral cavity showed that the qualitative composition of the microflora did not differ in all main groups studied by us and in the control group. The spectrum of detected microorganisms was represented as pathogenic as well as conditionally pathogenic microorganisms and fungi. The presented data between different types of oral microorganisms will help overcome the limitations of current treatments and identify new targets for the treatment of complex polymicrobial infections.

Taking into account the peculiarities of pathological changes and dysbiotic changes in the oral cavity of patients with viral hepatitis B and C and HIV-infection, it is necessary to develop and implement adapted schemes for individual oral hygiene, and the use of local probiotics in parallel with antiviral treatment of major diseases will lead to the correction of oral cavity microbiocenosis, depending on degree of dysbiotic shift.

Keywords: *microflora, oral cavity, HBV, HCV, HIV.*

Introduction

Viral hepatitis and human immunodeficiency virus (HIV) remain a major global public health problem. So, to date, HIV has claimed more than 35 million human lives [*WHO, 2016*]. Approximately 296 million people in the world live with

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Address for Correspondence:

Vahe Yu. Azatyan
Department of Therapeutic Stomatology Yerevan State Medical University
2 Koryun Street, Yerevan 0025, Armenia
Tel.: (+374 91) 32-67-73
E-mail: vahe.azatyan@gmail.com

chronic hepatitis B virus (HBV) infection and 58 million people have chronic hepatitis C virus (HCV) infection, with 1.5 million new infections each year [*WHO, 2021a*; *b*]. The number of people living with HIV in 2020 was about 1.5 million, the incidence number was 0.19 (0.13-0.27) per 1000 uninfected population [*WHO, 2021c*].

Armenia is a country with the below-average income and has 3-5% prevalence of HCV among the general population. For this indicator Armenia is on the 3rd place among the post-soviet countries [*Azatyan V et al., 2019*]. The prevalence of HBV in Armenia is 2% [*Azatyan V et al., 2019*].

The dentist is one of the first specialists to face the symptoms of oral lesions in viral hepatitis B, C and HIV [*Garbin C et al., 2014*].

The microbiota plays a key role in maintaining normal homeostasis, morphogenesis, metabolism and immune system function, which plays a crucial role for human health [*Morgan X et al., 2013*]. Oral microorganisms are the result of microorganisms persisting in them, including those coming from other econiches of the macroorganism [*El Aidy S et al., 2013*]. The oral cavity is a specific, complicated and stable microbiocinosis and is a favorable environment for the growth and maintenance of the vital activity of microorganisms [*Flemming H et al, 2019; Zaura E et al., 2019*]. Various tissues and organs of the human oral cavity, for example, such as teeth, gums, gingival grooves, the mucous membrane of the tongue, cheeks, the hard and soft palates, have noticeable differences in the composition of the microbial communities inhabiting them [*Dewhirst F et al., 2010; Zhao Y et al., 2018*].

To overcome it is possible, due to the uniting the knowledge and will of all doctors in the world

It is known that the oral microorganisms are constantly under the influence of immunoglobulins, which are formed in the salivary glands, and their production does not depend on the content of immunoglobulins in the blood serum. A correlation has been established between a number of pathogenic and opportunistic microorganisms in the oral cavity with the processes of local production, i.e. *in situ* immunoglobulins of class A and G, both in normal and pathological conditions [*Wilson T et al., 2014*]. The organs and tissues of the oral cavity are closely interconnected with the organs and systems of the human body as a whole. Therefore, various oral mucosal lesions are developed as a result of internal diseases [*Moyes D et al., 2016*]. The changes in the mucous membrane of the oral cavity and periodontium can be aggravated by accompanying systemic therapy, which leads to a decreased mucosal immunity of the macroorganism and, as a result, to dystrophic and degenerative changes in the oral cavity [*Gheorghe D et al., 2018; Back-Brito G et al., 2019; Černáková L et al., 2020*].

A series of works have been devoted to studying the state of the oral mucosa and periodontium, the microbial composition in HBV, HCV, HIV infections, in particular [*Anwar K et al., 2012; Chopra S, 2012; Ling Z et al., 2015; O'Brien S et al., 2017*]. So, in particular, dysbiotic changes in the oral cavity were revealed in patients with diffuse liver damage of viral etiology with periodontal pathology against the background of long-term in situ persistence of *Candida spp, Enterobacteriaceae* and *S. aureus* [*Laheij A et al., 2012; Desikan P et al., 2019*]. *Candida spp* affected 90% of HIV-infected patients [*Traboulsi R et al., 2008; Ribeiro A et al., 2017*]. The literary analysis shows that a rather narrow spectrum of microorganisms was studied in individual works.

The aim of this study was to examine the most frequently detected oral microorganisms in patients with viral hepatitis B, C and HIV-infection.

MATERIALS AND METHODS

The main study group included 135 patients who were divided into groups depending on the underlying infectious disease (I group hepatitis B virus n=45, group II hepatitis C virus n=45, III group HIV-infection n=45, IV group control group n=45) with oral mucosal lesions in the age range of 18-67 years, who were hospitalized in 2018 and 2019 in "Nork" Infection Hospital and "Armenicum" Medical Clinical Centre (Yerevan, Armenia). The control group involved 45 subjects without HBV, HCV and HIV-infection with oral mucosal lesions, who applied to Dental Clinic No 1 of Yere-

van State Medical University in the same period. Their age fluctuated from 20 to 69.

The viral nature of hepatitis and HIV was verified by the detection of hepatitis B virus deoxyribonucleic acid, hepatitis C virus ribonucleic acid and HIV in the blood serum of the examined subjects.

The samples taken with sterile tampons from the oral mucosa were used as the material for microbiological research. The tampons were immersed in tubes with 5 *ml* meat-peptone broth and delivered to the laboratory for research no later than 2 hours from the moment the material was taken. From the source material, bacterioscopy was performed to assess the general picture of the microflora and tenfold dilutions were prepared in meat-peptone broth. The diluted samples were inoculated by the drop method on selective and differential diagnostic media Endo agar, Salt Egg Yolk agar, Sabouraud, 5% blood agar. The incubation regime for the growth of microorganisms on solid selective and differential-diagnostic media was taken as follows: for Endo agar medium – 37° C for 24 hours, Salt Egg Yolk agar – 37°C for 24-48 hours, Sabouraund – 37°C for 48-72 hours, blood agar – 37°C for 24-48 hours respectively. The colonies grown on nutrient media when plated from maximum dilutions were subjected to group (for *Enterobacteria*), generic (for *Streptococcus, Candida spp*) and species (for *Staphylococcus*) identification. When assessing the quantitative growth of microorganisms involved in the occurrence of a regional infectious process, we used the general scheme of colony growth criteria: 10^2-10^3 – scanty growth (10-25 colonies); 10^4-10^5 – moderate growth (at least 50 colonies); 10^6-10^8 – abundant growth (colonies are not counted) (Order No 535 of the Ministry of Health of the USSR dated April 22, 1985 "On the unification of microbiological (bacteriological) research methods used in clinical diagnostic laboratories of medical institutions") [*Lagun L, 2016*]. Moderate and abundant growth of microorganisms is evident of the etiological role of this microorganism in the development of pathological manifestations of oral mucosa.

The final identification of microorganisms was carried out in accordance with the morphology of the colonies grown on selective nutrient media, and with the subsequent determination of the biochemical properties (enzymatic activity) of the corresponding microorganism [*Charousova I et al., 2017*].

Statistical analysis: Descriptive analysis was computed for all variables of interest. Differences between two groups were evaluated using "chi-square" or "Fisher's exact" tests for categorical variables and "Wilcoxon signed rank test" for continuous variables. Spearmen correlation was performed for determination of relationships between continuous variables. Analyses were conducted using Excel 2013, R software and program Vassar Stats to calculate Odds Ratio and 95% Confidence Intervals.

Results

We have studied the features of the formation of pathological biotopes in the oral cavity of patients with viral hepatitis B, C and HIV-infection.

The comparative analysis of the frequency and intensity of inoculation of individual microorganisms between the main groups and the control group is presented in tables 1

As can be seen from the tables, scanty growth of microorganisms was detected in the majority of control group patients. Obviously, this criterion is not a sign of the pathogenicity of a microorganism (see Methodology).

Actinomyces were examined separately and considered as different type of bacteria, as far as yeast-like fungi of the genus *Candida* (*Candida spp*) were also examined separately.

From the pathogenic microflora *S. aureus* and *Str. pyogenes* were sown more often (Fig. 1).

As can be seen in figure 1, patterns of detection of moderate and abundant growth of pathogenic microorganisms *S. aureus and Str. pyogenes* have the following picture. Moderate growth of *S. aureus* with HCV, p=0.38; OR = 1.78; 95% CI 0.75 to 4.2 and with HBV, p<0.005; OR=0.51; 95% CI 0.51 to 0.94, and *Str. pyogenes* had an identical picture, both in HBV and HCV (p<0.001; OR = 0.29; 95% CI, 0.14 to 0.59). Abundant growth of *S. aureus and Str. pyogenes* was not observed in both HBV and HCV. It should be noted that the rates of moderate growth of both microorganisms are lower in HIV-infection, which, in our opinion, is ex-

Table 1.

Microbial landscape of the oral cavity in patients with *HBV, HCB, HIV-infection and control groups*

Microorganisms	Level	Control group n=45 (%)	Viral hepatitis B				Viral hepatitis C				Human immunodeficiency virus Infection			
			HBV n=45 (%)	Odds Ratio	95% CI	p value	HCV n=45 (%)	Odds Ratio	95% CI	p value	HIV n=45 (%)	Odds Ratio	95% CI	p value
S. aureus	sg	20 (44.4)	0 (0)	Inf	4.16– Inf	p<0.001	14 (31.1)	0.57	0.24-1.34	p>0.48	11 (24.4)	1.49	0.65-3.43	p>0.34
	mg	25 (55.6)	45 (100)	0.51	0.27-0.94	p<0.005	31 (68.9)	1.78	0.75-4.2	p>0.38	20 (44.4)	1.02	0.5-2.08	p>0.95
	ag	0 (0)	0 (0)	-	-	N/R**	0 (0)	-	-	N/R**	14 (31.1)	0.01	0.0-0.27	p<0.001
Str. pyogenes	sg	31(68.9)	1 (2.2)	0.01	0.001-0.082	p<0.001	0 (0)	Inf	6.78-Inf	p<0.001	20 (44.4)	0.36	0.15-0.86	p>0.497
	mg	14 (31.1)	44 (97.8)	0.29	0.14-0.59	p<0.001	45 (100)	0.29	0.14-0.59	p<0.001	18 (40)	1.48	0.62-3.52	p>0.267
	ag	0 (0)	0 (0)	-	-	N/R**	0 (0)	-	-	N/R**	7 (15.6)	0.01	0.0-0.69	p=0.013
Enterococcus	sg	45 (100)	45 (100)	1	0.63-1.93	p>1	7 (15.5)	5.96	2.47-14.41	p<0.001	30 (66.7)	1.23	0.67-2.25	p>0.508
	mg	0 (0)	0 (0)	-	-	N/R**	38 (84.5)	0.01	0.0-0.1	p<0.001	15 (33.3)	0.01	0.0-0.28	p<0.001
	ag	0 (0)	0 (0)	-	-	N/R**	0 (0)	-	-	N/R**	0 (0)	-	-	N/R**
Veillonella	sg	45 (100)	21 (46.7)	1.95	1.02-3.71	p<0.001	16 (35.6)	2.61	1.31-5.18	p<0.001	12 (26.7)	3.07	1.45-6.49	p<0.001
	mg	0 (0)	24 (53.3)	0.01	0-0.16	p<0.001	22 (48.8)	0.01	0.0-0.18	p<0.001	28 (62.2)	0.01	0.0-0.13	p<0.001
	ag	0 (0)	0 (0)	-	-	N/R**	7 (15.6)	0.01	0.0-0.69	p=0.013	5 (11.1)	0.01	0.0-0.95	p=0.0219
Actinomyces	sg	40 (88.9)	21 (46.7)	0.11	0.04 – 0.33	p<0.001	17 (37.8)	0.08	0.03 -0.23	p<0.001	33 (73.3)	0.34	0.11-1.08	p>0.979
	mg	5 (11.1)	24 (53.3)	9.14	3.05 – 27.43	p<0.001	21 (46.6)	7.0	2.33 – 21.00	p=0.004	12 (26.7)	2.91	0.93-9.1	p=0.0669
	ag	0 (0)	0 (0)	-	-	N/R**	7 (15.6)	0.01	0.0-0.69	p=0.013	0 (0)	-	-	N/R**
E. coli	sg	45 (100)	23 (51.1)	1.78	0.95-3.35	p=0.003	11 (24.4)	3.79	1.77-8.12	p<0.001	11 (24.4)	3.35	1.55-7.21	p<0.001
	mg	0 (0)	4 (8.9)	0.01	0.0-1.45	p<0.05	19 (42.2)	0.01	0.0-0.21	p<0.001	22 (48.8)	0.01	0.0-0.18	p<0.001
	ag	0 (0)	18 (40)	0.01	0.0-0.22	p<0.001	15 (33.3)	0.01	0.0-0.28	p<0.001	12 (26.7)	0.01	0.0-0.32	p<0.001
Klebsiella	sg	45 (100)	23 (51.1)	1.78	0.95– 3.35	p=0.003	12 (26.7)	3.48	1.66-7.3	p<0.001	17 (37.8)	2.17	1.09-4.29	p<0.001
	mg	0 (0)	4 (8.9)	0.01	0.0-1.45	p<0.05	20 (44.4)	0.01	0.0-0.2	p<0.001	19 (42.2)	0.01	0.0-0.19	p<0.001
	ag	0 (0)	18 (40)	0.01	0.0-022	p<0.001	13 (28.9)	0.01	0.0-0.13	p<0.001	9 (20)	0.01	0.0-0.45	p=0.00125
Candida spp	sg	39 (86.7)	20 (44.4)	0.123	0.04 – 0.35	p<0.001	20 (44.4)	0.12	0.04 – 0.35	p<0.001	0 (0)	Inf	5.35-Inf	p<0.001
	mg	6 (13.3)	25 (55.6)	8.13	2.9 – 23.02	p<0.001	18 (40)	4.3	1.52 – 12.34	p=0.004	2 (4.4)	0.3	0.06-1.59	p>0.267
	ag	0 (0)	0 (0)	-	-	N/R**	7 (15.6)	0.01	0.0-0.69	p=0.013	43 (95.6)	0.01	0.0-0.08	p<0.001

Notes: *sg – scanty growth; mg – moderate growth; ag – abundant growth, inf – infinity, ** - N/R – No Result, P-volume tests result from the comparison between HBV, HCB, HIV and control groups.*

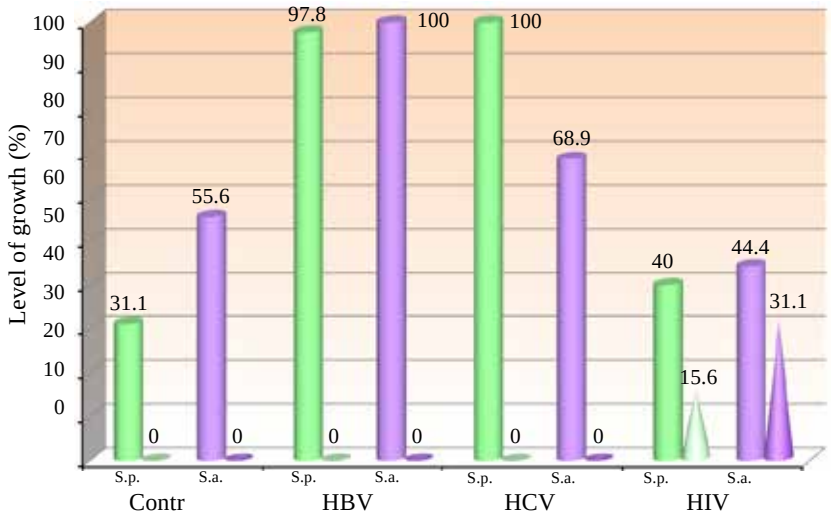

Figure 1. *Growth pattern of pathogenic microorganisms S. aureus (S.a.) and Str. pyogenes (S.p) with HBV, HCV and HIV-infection. Moderate growth (cylinders), abundant growth (cones)*

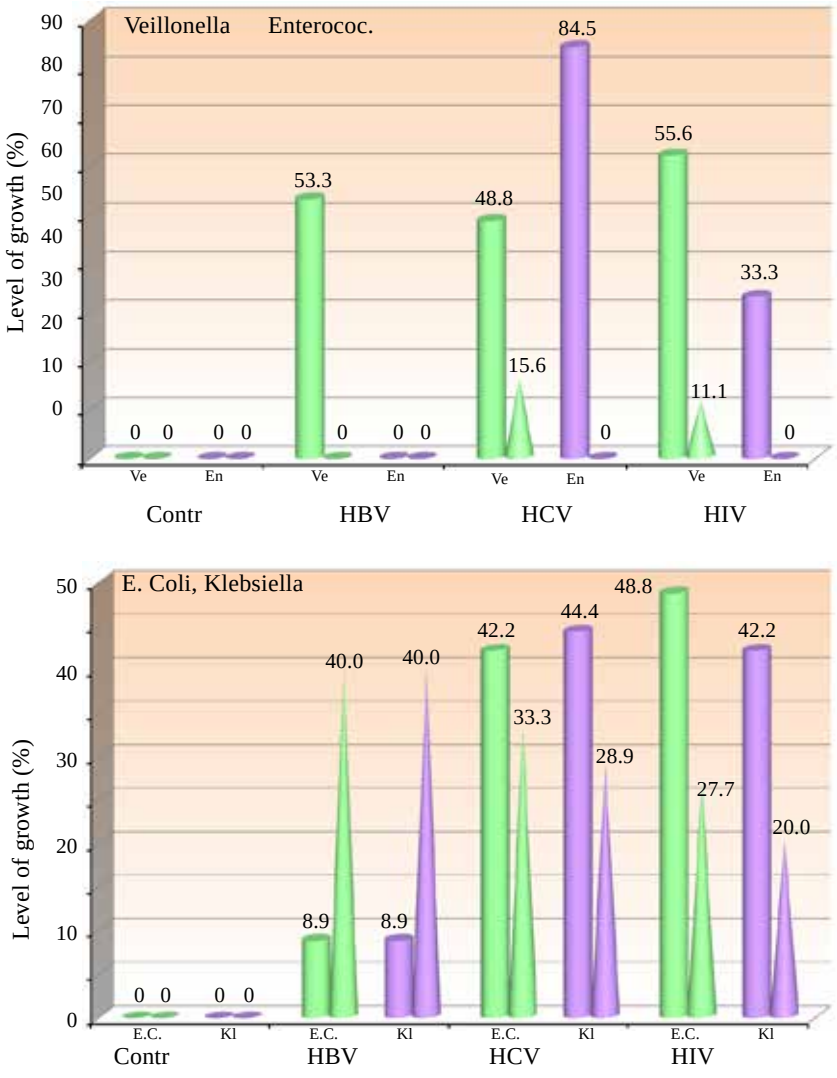

Figure 2. *Growth pattern of conditionally pathogenic microorganisms Enterococcus (A), Veillonella (B), E.coli (C) and Klebsiella (D) with HBV, HCV and HIV-infection. Moderate growth (cylinders), abundant growth (cones).*

plained by the detection of a significantly larger number of cases of abundant growth compared to the control (*S. aureus* in HIV-infection $p<0.001$; OR = 0.01; 95% CI, 0.0 to 0.27; *Str. pyogenes* in HIV-infection $p=0.013$; OR = 0.01; 95% CI, 0.0 to 0.69).

From conditionally pathogenic microorganisms *Enterococcus*, *Veillonella*, *E.coli* and *Klebsiella* were sown most often (Fig. 2).

As can be seen in figure 2, *Enterococcus* behaved most favorably of all microorganisms, the growth of which was scanty (100%) in all patients of the control group and HBV patients. It was detected more often in HCV and HIV-infection comparing with control group ($p<0.001$). *Veillonella* behaves somewhat more aggressively than *Enterococcus*, which, significantly compared to the control group (HCV: $p<0.001$; OR=0.01; 95% CI, 0.0 to 0.18 and HIV-infection: $p<0.001$; OR=0.01; 95% CI, 0.0 to 0.13) showed moderate growth in all major groups (including those with HBV: $p<0.001$; OR=0.01: 95% CI, 0.0 to 0.16), and also, abundant growth in HCV ($p=0.013$; OR=0.01; 95% CI, 0.0 to 0.69) and in HIV-infection ($p=0.0219$; OR=0.01; 95% CI, 0.0 to 0.95). *E.coli* and *Klebsiella* display practically the same concerning pathogenicity. All examined criteria of the growth (moderate and abundant), with high degree of authenticity practically identical as compared with the control group ($p<0.001$), except the moderate growth in HBV in which the difference of the data compared with the control is with low degree of significance ($p<0.05$; OR=0.01; 95% CI, 0.0 to 1.45). Compared with the indicators of all four conditionally pathogenic microorgan-

isms, it is clearly seen that in all the main groups the abundant growth of *E.coli* and *Klebsiella* is the most pronounced.

We also studied the fungi *Actinomyces* and *Candida spp*, which were also often sown from the oral cavity (Fig. 3).

When analyzing the data of *Actinomyces* and *Candida spp*, moderate growth was revealed in all the groups, with a high degree of reliability compared with the control group in patients with HBV ($p<0.001$; *Actinomyces* OR=9.14; 95% CI, 3.05 to 27.43; *Candida spp* OR=8.13; 95% CI, 2.9 to 23.02) and HCV (p=0.004; *Actinomyces* OR=7.0; 95% CI, 2.33 to 21.0; *Candida spp* OR=4.3; 95% CI, 1.52 to 12.34). In the group of patients with HIV-infection, the difference in data is statistically insignificant when detecting *Actinomyces* (p=0.0669; OR=2.91; 95% CI, 0.93 to 9.1) and *Candida spp* (p=0.267; OR=0.3; 95% CI, 0.06 to 1.59), the abundant growth was found in patients with HCV (p=0.013; OR =0.01; 95% CI, 0.0 to 0.69). The presence of abundant growth of *Candida spp* in HIV-infection is very clearly seen ($p<0.001$; OR=0.01; 95% CI, 0.0 to 0.08).

Discussion

There is a homeostatic balance between the resident oral microbiota and the host. The disruptions of microbiota of the oral cavity in certain conditions can promote the growth of **"**non-oral**"** pathogens which are difficult to eliminate because of their higher stability to antimicrobial preparations which increase the probability of none- effectiveness of treatment and repeated infection. The presence of these bacteria in the oral cavity has been proved to be associated with several oral diseases such as periodontitis, caries, and gingivitis, as well as systemic diseases important to clinical medicine, such as cystic fibrosis, HIV, rheumatoid arthritis, and others [*Huh J, Roh T, 2020*]. However, the question of whether these species are simply temporary members or pathogens to the oral cavity still remains controversial [*Lee Y et al., 2021; Zaatout N, 2021*]. An imbalance in the microbial flora promotes the growth of various clinically important pathogens commonly considered to be "non-oral" bacteria, such as gram-negative *E. coli*, *Enterococcus* and *Staphylococcus* [*Van Winkelhoff A et al., 2016*]. Studies have shown that they can occur in high numbers and move from transient species to oral colonizers in individuals with weak immunity [*Arirachakaran P et al., 2016; Simões-Silva L et al, 2018*]. However, some studies have shown that they can also colonize healthy people [*Ranganathan A et al., 2017; Chinnasamy A et al., 2019*]. Moreover, systemic colonization and infections associated with extra-oral bacteria (spherical - cocci and convoluted - spirilla and vibrios), isolated from the oral cavity have been identified [*Arirachakaran P et al., 2016; Ghapanchi J et al., 2019*], which makes the oral cavity a non -hospital reservoir [*Kearney A et al., 2020*].

As mentioned above, there are practically no works in the literature where a comparative analysis of the microbial composition in HBV, HCV and HIV has been carried out. Single works are devoted to the study of the state of the microflora of the oral cavity in other diseases [*Esaian M et al., 2021*]. It should be noted that the authors did not use the criteria for assessing the quantitative growth of microorganisms and brought only descriptive analysis indicators. We also used these criteria, since only moderate and abundant growth indicates the etiological role of this microorganism in the development of pathological manifestations of the oral mucosa. In a microbiological study in patients with systemic sclerosis in a large

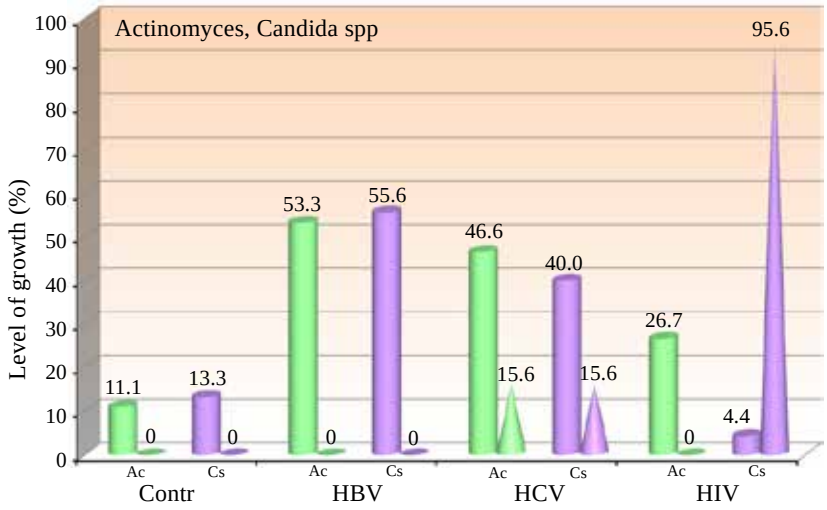

Figure 3. *Growth pattern of Actinomyces (Ac) and Candida spp (Cs) with HBV, HCV and HIV-infection. Moderate growth (cylinders), abundant growth (cones)*

number in the same percentage of cases (18.9%), pathogenic *S. aureus* and *Candida albicans*, *S. viridans* (in 15%) were detected, while *Candida albicans* was detected 3 times more often than in the control (p=0.049), *Veillonella* were also detected in significant numbers [*Esaian M et al., 2021*]. In our work, abundant growth of *S. aureus* (31.1%) and *S. pyogenes* (15.6%) was detected only in HIV, *Candida spp* (15.6% and 95.6%) and *Veillonella* (15.6%, 11.1%) – for HCV and HIV, respectively.

Today, 14 species of *Veillonella* are known, seven of which can be isolated from the human oral cavity. In connection to similar biochemical and phenotypic characteristics, the identification of *Veillonella* species currently is mainly based on differences in genes [*Aujoulat F et al., 2014; Mashima I et al., 2018; Luo Y et al., 2020*]. Due to the fact that genetic studies are not available, and the purpose of our work was not to study certain strains of *Veillonella*, we limited ourselves only to its determination in the pathologies we studied. Moderate growth of *Veillonella* was determined in all major groups, while abundant growth of the latter was characteristic of HCV and HIV (15.6%; 11.1%, respectively). *Veillonella parvula* is an anaerobic commensal and conditionally pathogenic microorganisms whose ability to attach to surfaces or other bacteria and form biofilms is important in order to colonize complex human microbial communities such as the gut and oral microbiota [*Béchon N et al., 2020*]. Taking into consideration this fact, we will review our data below when describing polymicrobial interactions.

Fungi of the genus *Candida*, constituting a significant part of the biocenosis of the macroorganism [*Neville B et al., 2015*], interact with other types of conditionally pathogenic microorganisms and representatives of the normal flora. The colonization process of *Candida spp* in the human body is partly regulated by immune factors [*Martins N et al., 2014*]. Representatives of the *Candida* genus are typical causative agents of opportunistic infections and multiply their pathogenic potential under conditions of disturbances in the host's immune system, as a result of which they can not only worsen the prognosis of the underlying disease in HIV-infected patients, but also be the cause of lethal effect [*Pang W et al., 2018*]. Our results obviously correlate with the validity of the data given by the above authors. Thus, abundant growth of *Candida spp* was detected with a high degree of certainty in 15.6% of patients with HCV (p=0.013) and in 95.6% of patients with HIV (p<0.001), which is a very convincing example of the presence of immunodeficiency in these patients.

Unfortunately, the analysis of the literature shows that most of the works are experimental and are devoted to polymicrobial interactions, especially between commensal species with high pathogenic potential [*Kong E et al., 2015, 2016; Schlecht L et al., 2015; Todd O et al., 2019; Zainal M et al., 2021*]. In clinical practice, these issues remain largely understudied.

In microbial communities, fungi of the genus *Candida* not only experience antagonistic pressure from representatives of the normal microflora, but often form associations with other microorganisms, which, on the contrary, contribute to the colonization of biotopes by fungal flora. Experimental work by Kong E.F. and co-authors (2015) show that although the dimorphic fungal species *Candida albicans* and the bacterium *S. aureus* are common human colonizers, they are considered the leading conditionally pathogenic microorganisms. In particular, oral candidiasis, characterized by hyphae invasion of the oral mucosal tissue, is the most common opportunistic infection in HIV-positive and immunocompromised individuals. The obtained data showed that in mice with oral candidiasis, subsequent exposure to *S. aureus* led to a systemic bacterial infection with high morbidity and mortality [*Kong E et al., 2015*]. In vitro and ex vivo results demonstrate specific binding of *Staphylococcus* to *Candida* hyphae elements [*Schlecht L et al., 2015*]. Our data show that, in parallel, the highest rates of abundant growth of *S. aureus* (31.1%) and *Candida spp* (95.6%) are observed in patients with HIV, in which there is the most pronounced immunodeficiency. At the same time, in patients with viral hepatitis B, a moderate increase in *Candida spp* (55.6%) was observed, and in patients with viral hepatitis C, both moderate growth (40%) and abundant growth (15.6%) were observed, which indicates a less pronounced decrease in immunity, which proves the absence of chronic pseudomembranous candidiasis of the oral cavity in patients with viral hepatitis.

A number of works are devoted to polymicrobial interactions of *Veillonella* and *Streptococci* [*Mashima I, Nakazawa F, 2014; Ghapanchi J et al., 2019*]. Thus, according to Luo Y.X. and colleagues (2020) in the conditions of saliva flow in the oral cavity, adherence of *Streptococci* provides a place for *Veillonella*, and in the absence of *Streptococci*, *Veillonella* cannot attach and grow.

According to the results of our research, the abundant growth of *S. pyogenes* (15.6%) and *Veillonella* (11.1%) are observed almost equally in patients with HIV infection, which can be judged by the diverse picture of the microbial geography of the oral cavity, on the one hand, and are not characteristic microorganisms in the development of candidal stomatitis in this group patients, on the other hand.

The works concerning the prospects for treatment in the presence of polymicrobial interactions are of particular interest. Thus, Kong E.F. and co-authors (2016) showed that, when grown together, fungi provide the bacteria increased tolerance to antimicrobials. This process is mediated by polysaccharides released by the fungal cell into the surrounding environment. The biofilm matrix formed by these polysaccharides prevents the penetration of drugs and provides the protection bacteria [*Kong E et al., 2016*].

One of the limitations of the study was that, research participants with HBV, HCV and HIV-infection were included from "Nork" Clinical Hospital of Infectious Diseases and "Armenicum" Clinical Center registry and with consideration of their agreement to participate, we encountered with limitation for larger sample selection.

Conclusion

Understanding the patterns of interaction between different types of oral microorganisms will help overcome the limitations of current treatments and identify new targets for the treatment of complex polymicrobial infections. Taking into account the peculiarities of pathological changes and dysbiotic changes in the oral cavity in patients with viral hepatitis B, C and HIV-infection, it is necessary to develop and implement adapted schemes for individual oral hygiene and the use of local probiotics in parallel with antiviral treatment of major diseases will lead to the correction of oral cavity microbiocinosis, depending on degree of dysbiotic shift.

REFERENCES

1. *Anwar KP, Malik A, Subhan KH (2012).* Profile of candidiasis in HIV infected patients. Iran J Microbiol. 4(4): 204-209
2. *Arirachakaran P, Poovorawan Y, Dahlén G (2016).* Highly-active antiretroviral therapy and oral opportunistic microorganisms in HIV-positive individuals of Thailand. J Investig Clin Dent. 7(2): 158-167
3. *Aujoulat F, Bouvet P, Jumas-Bilak E, Jean-Pierre H, Marchandin H (2014).* Veillonella *seminalis sp. nov*., a novel anaerobic Gram-stain-negative coccus from human clinical samples, and emended description of the genus Veillonella. Int J Syst Evol Microbiol. 64(10): 3526-3531
4. *Azatyan V, Yessayan L, Shmavonyan M, Melik-Andreasyan G, Perikhanyan A, Porksheyan K (2019).* Evaluation of IL-2, IL-10, IL-4 and ɤ-interferon levels in the oral fluids of patients with hepatitis C, B and HIV. J Infect Dev Ctries. 13(5.1): 069S-074S
5. *Back-Brito GN, Mota AJ, Vasconcellos TC, Querido SMR, Jorge AOC., et al (2009).* Frequency of Candida spp. in the Oral Cavity of Brazilian HIV-Positive Patients and Correlation with CD4 Cell Counts and Viral Load. Mycopathologia. 167(2): 81-87
6. *Béchon N, Jiménez-Fernández A, Witwinowski J, Bierque E, Taib N., et al (2020).* Autotransporters Drive Biofilm Formation and Autoaggregation in the Diderm Firmicute *Veillonella parvula*. J Bacteriol. 202(21): e00461-20
7. Černáková L, Rodrigues CF (2020). Microbial interactions and immunity response in oral *Candida* species. Future Microbiol. 15: 1653-1677
8. *Charousova I, Medo J, Halenarova E, Javorekova S (2017).* Antimicrobial and enzymatic activity of actinomycetes isolated from soils of coastal islands. J Adv Pharm Technol Res. 8(2): 46-51
9. *Chinnasamy A, Ramalingam K, Chopra P, Gopinath V, Bishnoi GP, Chawla G (2019).*

Chronic nail biting, orthodontic treatment and *Enterobacteriaceae* in the oral cavity. J Clin Exp Dent. 11(12): e1157-e1162

10. *Chopra S, Arora U (2012).* Skin and mucocutaneous manifestations: useful clinical predictors of HIV/AIDS. J Clin Diagn Res. 6(10): 1695-1698
11. *Desikan P, Rangnekar A, Khan Z, Panwalkar N, Bose P, Gulwani HV, Kaur S (2019).* Sero-occurrence of HBV/HCV co-infection and levels of liver enzymes among patients at a tertiary care hospital in central India: a pilot study. Cent Asian J Glob Health. 8(1): 313
12. *Dewhirst FE, Chen T, Izard J, Paster BJ, Tanner AC., et al (2010).* The Human oral microbiome. J Bacteriol. 192(9): 5002-5017
13. *El Aidy S, Hooiveld G, Tremaroli V, Bäckhed F, Kleerebezem M (2013).* The gut microbiota and mucosal homeostasis: colonized at birth or at adulthood, does it matter? Gut Microbes. 4(2): 118-124
14. *Esaian MS, Selifanova EI, Margarian EG, Beketova TV (2021).* [State of oral microflora in patients with systemic scleroderma] [Published in Russian]. Sovremennaia revmatologiia. 15(5): 39-43
15. *Flemming HC, Wingender J (2010).* The biofilm matrix. Nat Rev Microbiol. 8(9): 623-633
16. *Garbin CA, de Souza NP, de Vasconcelos RR, Garbin AJ, Villar LM (2014).* Hepatitis C virus and dental health workers: an update. Oral Health Prev Dent. 12(4): 313-321
17. *Ghapanchi J, Emami A, Rezazadeh F, Shakibasefat H, Pirbonyeh N (2019).* Isolation of Enterococcus faecalis in the saliva samples of patient candidates for liver transplantation. Dent Res J (Isfahan). 16(5): 333-337
18. *Gheorghe DN, Foia L, Toma V, Surdu A, Herascu E., et al (2018).* Hepatitis C infection and periodontal disease: is there a common immunological link? J Immunol Res. 2018: 8720101
19. *Huh JW, Roh TY (2020). Opportunistic detection of Fusobacterium nucleatum as a marker for the early gut microbial dysbiosis. BMC Microbiol. 20(1): 208*
20. *Kearney A, Kinnevey P, Shore A, Earls M, Poovelikunnel TT., et al (2020).* The oral cavity revealed as a significant reservoir of Staphylococcus aureus in an acute hospital by extensive patient, healthcare worker and environmental sampling. J Hosp Infect. S0195-6701(20): 30103-30111
21. *Kong EF, Kucharíková S, Dijck PV, Peters BM, Shirtliff ME, Jabra-Rizk MA (2015).* Clinical Implications of Oral Candidiasis: host tissue damage and disseminated bacterial disease. Infect Immun. 83(2): 604-613
22. *Kong EF, Tsui C, Kucharíková S, Andes D, Dijck PV, Jabra-Rizk MA (2016).* Commensal protection of Staphylococcus aureus against antimicrobials by Candida albicans biofilm matrix. mBio. 7(5): e01365-16
23. *Lagun LV (2016).* [Methods of microbiological research] [Published in Russian]. Teaching aid for students of 2-3 courses of medical and medical-diagnostic faculties of medical universities. Gomel. 164p
24. *Laheij AM, Kistler JO, Belibasakis GN, Välimaa H, de Soet JJ (2012).* Healthcare-associated viral and bacterial infections in dentistry. J Oral Microbiol. 4: 17659
25. *Lee YH, Chung SW, Auh QS, Hong SJ, Lee YA., et al (2021).* Progress in oral microbiome related to oral and systemic diseases: an update. Diagnostics (Basel). 11(7): 1283
26. *Ling Z, Liu X, Cheng Y, Jiang X, Jiang H, Wang Y, Li L (2015).* Decreased Diversity of the Oral Microbiota of patients with hepatitis B virus-induced chronic liver disease: a pilot project. Sci Rep. 5: 17098
27. *Luo YX, Sun ML, Shi PL, Liu P, Chen YY, Peng X (2020).* Research progress in the relationship between Veillonella and oral diseases. Hua Xi Kou Qiang Yi Xue Za Zhi. 38(5): 576-582
28. *Martins N, Ferreira IC, Barros L, Silva S, Henriques M (2014).* Candidiasis: predisposing factors, prevention, diagnosis and alternative treatment. Mycopathologia. 177(5-6): 223-240
29. *Mashima I, Djais AA, Haase EM, Scannapieco FA, Otomo M, Saitoh M, Nakazawa F (2018).* Establishment of a species-specific primer pair for detecting Veillonella infantium based on the 70 kDa heat shock protein gene dnaK. Anaerobe. 52: 79-82
30. *Mashima I, Nakazawa F (2014).* The influence of oral *Veillonella* species on biofilms formed by Streptococcus species. Anaerobe. 28: 54-61

31. *Morgan XC, Segata N, Huttenhower C (2013).* Biodiversity and functional genomics in the human microbiome. Trends Genet. 29(1): 51-58
32. *Moyes D, Islam A, Kohli A, Naglik J (2016).* Oral epithelial cells and their interactions with HIV-1. Oral Dis. 22(1): 66-72
33. *Neville BA, d´Enfert C, Bougnoux ME (2015).* Candida albicans commensalism in the gastrointestinal tract. FEMS Yeast Res. 15(7): fov081
34. *O'Brien SF, Yi QL, Fan W, Scalia V, Goldman M, Fearon MA (2017).* Residual risk of HIV, HCV and HBV in Canada. Transfus Apher Sci. 56(3): 389-391
35. *Pang W, Shang P, Li Q, Xu J, Bi L, Zhong J, Pei X (2018).* Prevalence of opportunistic infections and causes of death among hospitalized HIV-infected patients in Sichuan, China. Tohoku J Exp Med. 244(3): 231-242
36. *Ranganathan AT, Sarathy S, Chandran CR, Iyan K (2017).* Subgingival prevalence rate of enteric rods in subjects with periodontal health and disease. J Indian Soc Periodontol. 21(13): 224-228
37. *Ribeiro AL, de Alencar Menezes TO, de Melo Alves-Junior S, de Menezes SAF, Marques-da-Silva SH, Vallinoto ACR (2015).* Oral carriage of Candida species in HIV-infected patients during highly active antiretroviral therapy (HAART) in Belém, Brazil. Oral Surg Oral Med Oral Pathol Oral Radiol. 120(1): 29-33
38. *Schlecht LM, Peters BM, Krom BP, Freiberg JA, Hänsch GM (2015).* Systemic Staphylococcus aureus infection mediated by Candida albicans hyphal invasion of mucosal tissue. Microbiology (Reading). 161(1): 168-181
39. *Simões-Silva L, Ferreira S, Santos-Araujo C, Tabaio M, Pestana M., et al (2018).* Oral colonization of *Staphylococcus* species in a peritoneal dialysis population: a possible reservoir for PD-related infections? Can J Infect Dis Med Microbiol. 2018: 5789094
40. *Todd OA, Peters BM (2019).* Candida albicans and Staphylococcus aureus pathogenicity and polymicrobial interactions: lessons beyond koch's postulates. J Fungi (Basel). 5(3): 81
41. *Traboulsi RS, Mukherjee PK, Ghannoum MA (2008).* In vitro activity of inexpensive topical alternatives against Candida spp. isolated from the oral cavity of HIV-infected patients. Int J Antimicrob Agents. 31(3): 272-276
42. *Van Winkelhoff AJ, Rurenga P, Wekema-Mulder GJ, Singadji ZM, Rams TE (2016).* Non-oral gram-negative facultative rods in chronic periodontitis microbiota. Microb Pathog. 94: 117-122
43. *Wilson TG, Valderrama P, Rodrigues DBC (2014).* The case for routine maintenance of dental implants. J Periodontol. 85(5): 657-660
44. *World Health Organization (WHO) (2016).* Global health sector strategy on viral hepatitis 2016-2021. Towards ending viral hepatitis. Retrieved from: https://apps.who.int/iris/bitstream/handle/10665/246177/WHO-HIV-2016.06-eng.pdf
45. *World Health Organization (WHO) (2021a).* World Hepatitis Alliance. Hepatitis B. Retrieved from: https://www.who.int/news-room/fact-sheets/detail/hepatitis-b
46. *World Health Organization (WHO) (2021b).* World Hepatitis Alliance. Hepatitis C. Retrieved from: https://www.who.int/news-room/fact-sheets/detail/hepatitis-c
47. *World Health Organization (WHO) (2021c).* Global Health Workforce Statistics. Global health observatory data repository. Retrieved from: https://apps.who.int/gho/data/node.main.HIVINCIDENCE?lang%20=%20en
48. *Zaatout N (2021).* Presence of non-oral bacteria in the oral cavity. Arch Microbiol. 203(6): 2747-2760
49. *Zainal M, Zain NM, Amin IM, Noryati AV (2021).* The antimicrobial and antibiofilm properties of allicin against Candida albicans and Staphylococcus aureus – a therapeutic potential for denture stomatitis. Saudi Dent J. 33(2): 105-111
50. *Zaura E, Keijser BJ, Huse SM, Crielaard W (2009).* Defining the healthy "core microbiome" of oral microbial communities. BMC Microbiol. 9: 259
51. *Zhao Y, Mao YF, Tang YS, Ni MZ, Liu QH., et al (2018).* Altered oral microbiota in chronic hepatitis B patients with different tongue coatings. World J Gastroenterol. 24(30): 3448-3461

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Armen A. Muradyan

Address for correspondence:

Yerevan State Medical University
2 Koryun Street, Yerevan 0025,
Republic of Armenia

Phones:

(+37410) 582532 YSMU
(+37493 588697 Editor-in-Chief
Fax: (+37410) 582532
E-mail: namj.ysmu@gmail.com, ysmiu@mail.ru
URL: http//www.ysmu.am

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Armenia, 0018, Yerevan,
Tigran Mec 48, 43
Phone: (+374 91) 19 29 00,
E-mail: armana6@mail.ru