

LETTER TO THE EDITOR

The prevalence of human papillomavirus in patients with oral lichen planus and normal oral mucosaV. RADOCHOVÁ¹, L. PLÍŠKOVÁ², R. SLEZÁK¹

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Oral lichen planus (OLP) is a chronic inflammatory disorder that affects the oral mucous membrane. The prevalence of OLP in the population is considered to be 1%–2% (1). The etiology of OLP is not known. The immune system very probably plays the primary role in the development of this disease. During the last decades, several studies have suggested that human papillomaviruses (HPVs) are involved in the development of premalignant and malignant lesions (2). The causal role of HPV has been reported for OLP and oral squamous cell carcinoma, but there are wide variations in disease prevalence with regard to different geographic populations (3). The aim of this study was to determine the prevalence of HPV on the mucosa in patients with OLP and compare it with healthy mucosa.

Study protocol has been approved by the local ethical committee. Written informed consent was obtained from all subjects entering the study. Patients with OLP were included based upon following criteria: clinically diagnosed OLP according to objective examination (single physician) and histologically confirmed OLP. OLP was classified according to criteria previously published by World health Organization and modified by van der Meij *et al.* (4). Smokers and patients with alcohol abuse history were excluded from the

study. Sex- and age-matched controls were chosen from individuals undergoing various dental procedures with no known mucosal disease. Native tissue samples were sent for HPV genome detection. HPV DNA was extracted from native tissue. All samples were screened for the presence of HPV DNA by PCR amplification with primers GP5+/GP6+ located within the HPV L1 gene. The sequences of the forward and reverse primers used were FW (GP5+): 5'-TTTGTACTGTGGTAGACTACTAC-3' and REV (GP6+): 5'-AAAAATAAACTGTAAATCATATT-3'. This allows the detection of 37 HPV types, specifically 6, 11, 16, 18, 26, 31, 33, 35, 39, 40, 42, 45, 51, 52, 53, 54, 55, 56, 58, 59, 61, 62, 64, 66, 67, 68, 69, 70, 71, 72, 73 (MM9), 81, 82 (MM4), 83 (MM7), 84 (MM8), IS39, and CP6108. HPV typing was performed, however, due to low amounts of DNA it was not possible to analyze the results. Chi-square and Student t-test were used for comparisons. P value <0.05 was considered statistically significant. A total of 45 patients with confirmed diagnosis of OLP were examined for HPV, of whom, 33 (73.3%) were woman and 12 (26.7%) were men. The mean age of the patients was 56 years (± 14.96) with an overall range of 33–77 years. The control group consisted of 24 individuals, 19 (79.2%) were women and 5 (20.8%) were men. The mean age of the individuals in control group was 56.1 years (± 11.41) with an overall range of 29–81 years. There was no statistical significance according to age ($p = 0.96$) and gender ($p = 0.59$) between OLP patients and controls. There were 24 (53.3%) HPV-positive patients with OLP and 21 (46.7%) patients were HPV-negative. In the control group there were 12 sub-

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Abbreviations: HPV(s) = human papillomavirus(es); OLP = oral lichen planus

jects HPV-positive and 12 subjects HPV-negative. It means that 50% were positive and 50% were negative. There was no statistically significant difference between HPV prevalence in the control group and in the OLP group ($p = 0.79$). Of the HPV-positive patients with OLP, there were 8 men and 16 women and HPV-negative were 4 men and 17 women. No statistically significant difference was seen between men and women ($p = 0.28$). The patients with OLP were divided into two groups according to clinical types: the first group consisted of white forms OLP (reticular and plaque like), which included 29 patients and the second group consisted of red forms OLP (erythema and erosive lesions), which included 16 patients. HPV positivity was seen in 16 (55.2%) patients with reticular and plaque like lesions and in 8 patients with erythematous and erosive lesions (50%) (data is summarized in Table 1).

HPV infection in humans is common sexually transmitted disease with clear relation to premalignant and malignant lesions in cervix (5). The importance of HPV infection in oral cavity is much less clear. A review regarding this topic has been published in 2011 (6). It is a large-scale analysis of more than 2000 patients, which suggests that premalignant and potentially malignant oral lesions are related to HPV positivity. The odds ratio for OLP being HPV-positive was found to be 5.12, whereas in oral squamous cell carcinoma it was 3.98. In an Italian study it was estimated that there is a 7.8-times higher risk of HPV in oral premalignant lesions than in normal mucosa (7). A study from Hungary reported 32.8% of HPV-positive OLP lesions (3). The same group later reported percentage of HPV-positive OLP to be 19.7% (8). This relatively high prevalence of HPV in OLP lesions was not seen in Thai data by Arirachakaran and colleagues, where only 2.7% of lesions were positive for HPV (9). This fact suggests that there are probably huge geographic differences in incidence and prevalence of HPV infection in oral mucosal disorders worldwide. Our data have shown 53.3% HPV positive samples in OLP patients. This number is relatively high compared to data presented by previously mentioned studies. There was no difference between gender, age or oral lesion type (red versus white) in our patients. This observation is similar to those reported by two other groups (8, 10). This very recent report shows 70% of patients with OLP being positive for HPV-16. Only one small sample of patients showed higher prevalence of HPV in erosive lichen (11). Mattila and coworkers (12) have reported 15.9% of HPV-positive patients with atrophic OLP. In our study, extremely high incidence of HPV-positive samples was found in normal oral mucosa (50%). The incidence of HPV-positivity in recently published studies on similar topic was usually ranged from 0% to 7.3%. A Japanese study (13) reported higher HPV positivity. Data from Brazil, on the other hand, show that there was not a single case of HPV in healthy mucosa (14). The age of subjects in this study,

Table 1. Prevalence of HPV positivity in various groups

	Red	White	P value
HPV+	16	8	
HPV-	8	8	0.74
	Males	Females	
HPV+	8	16	
HPV-	4	17	0.28
	OLP	Control	
HPV+	24	12	
HPV-	21	12	0.79
	OLP	Control	
HPV+	12	5	
HPV-	33	19	0.59

however, was between 20–31 years and all were university students, which suggests that a higher socioeconomic status may play a role in these findings. In contradiction with these results, another study reported as much as 23.2% of HPV-positive samples from normal oral mucosa (15). A very large study in USA detected HPV DNA in oral rinses in 7.3% of 4846 subjects included (16). Recently, a different US study focused on HPV prevalence in females in cervix and in the oral cavity. It was shown that 42.7% of women have HPV in cervix but only 3.8% in oral cavity. Only 3% of females have positive results both in cervix and in oral mucosa (17). Huge geographic differences in HPV positivity clearly exist. Why the sample population has such a high prevalence of HPV DNA in healthy oral mucosa remains unclear and at present time there is no explanation. No larger trial has been conducted so far to identify HPV prevalence in healthy mucosal membrane in the Czech Republic. We were, therefore, not able to show any difference in HPV prevalence in the OLP lesions compared to healthy population. From this point of view it seems unlikely that HPV plays any major role in the pathogenesis of OLP. It is possible that the presence of HPV carries higher risk of developing oral lesions, however, direct connection to OLP remains to be elucidated.

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