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Clinical, Cytological and Genotypic Correlation between Oral Mucosa and Lower Genital Tract Lesions Related to HPV Infection in Women

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Abstract: ***To determine oral-genital coinfection with HPV in female patients who presented lesions suggestive of oral and genital HPV infection. Study design: 76 female patients, who attended Department of Oral Medicine of the School of Dentistry of the University of Buenos Aires were included. Oral clinical inspection, exfoliative cytology and nested polymerase chain reaction and subsequent sequencing (PCR) for HPV were performed. The 76 women were referred to the Department of Lower Genital Tract (TGI) of the José de San Martin Hospital for their gynecological study to search for lesions compatible with HPV infection by colposcopy, Pap smear and PCR. Correlation / regression coefficient and relative risk were estimated. Results: 39 positive oral lesions were found with PCR. Of the 76 patients with lesions suggestive of oral HPV, 11 patients also had lesions compatible with the virus in the lower genital tract. Only 10 lesions were positive for HPV at this location. There was coincidence in three oral-genital cases. Two patients had the same HPV genotype and one had different genotypes. Conclusions: In this study the percentage of oral-genital HPV coinfection was 27.27%. This suggests that oral HPV is not a predisposing factor for genital infection in the same patient.***

Keywords: HPV, Oral Mucosa, Genital tract, PCR.

1. Introduction

The prevalence of oral HPV and head and neck cancer (HNC) positive for HPV has increased significantly in the last 20 years [1, 2], this is due to a change in the incidence of HPV and HNC, to an improvement in the detection of HPV in tumor cells and a true increase in cancer associated with HPV (especially in the head and neck region). Although the prevalence of oral HPV infection is 5 to 10 times lower than in the genital region, high-risk HPV transmission is highly related to sexual activity [3]. For example, the risk of contracting HPV is very high greater in sexually initiated persons than in those without sexual experience; Similarly, oral HPV infection is strongly associated with early sexual onset, multiple sexual partners, open mouth kisses and oral sex both orally-orally and orally-genitally. [4, 5, 6]

Additional risk factors such as tobacco use, marijuana and alcohol consumption have been linked to oral HPV transmission; All these factors may be correlated with sexual activity.

According to one study, the increase in the prevalence of human papillomavirus in oral tumors can be considered as an epidemic [7]. Although the incidence of cervical cancer is decreasing, oral cavity cancer and HPV-associated oropharyngeal cancer is increasing. The presence of certain HPV genotypes could be a predictor of oral cancer, however, HPV-associated lesions may be less aggressive and exhibit a higher survival rate.

The incidence of oral HPV infection is within the same range in men and women, although the prevalence of oral HPV in men has been mostly reported [8]. The oncogenicity of HPV is thought to be similar in oral and cervix cancer, although there are many doubts about the risk factors that influence the progression of oral infection to oral neoplasma.

Although the incidence of HPV infection in non-cervical sites seems high, the high HPV clearance capacity observed in them can contribute to a low rate of this type of cancers. Although high-risk HPV infection is common in 80% of women who will become infected at some point in their lives, cervical cancer appears only rarely as a result of the infection. Most infections are eliminated as a result of a cell-mediated immune response and there is not much time for genetic deregulation and an accumulation of secondary gene errors.

HPV 16 has a higher risk of carcinogenicity because its persistence is greater than that of high-risk HPV genotypes.
It was found that smoking tobacco strongly increases the chances of persistence of HPV infections in the oral cavity but not in the genitals[9]. The oral cavity is more exposed than the cervix to tobacco chemicals, so the dose of toxins will be higher.

Smoking tobacco is independently associated with the risk of cervical cancer in case-control studies, and the risk of cervical dysplasia among women infected with HPV increases with the intensity and duration of tobacco use. However, it is not clear whether this risk is due solely to the genotoxic effects of tobacco-related carcinogens or if exposure to tobacco also affects the natural history of cervical HPV infection[12,13]. Immune dysfunction related to tobacco could facilitate an HPV infection in exposed individuals, prevent the possibility of eliminating an infection or facilitate the reactivation of a latent infection. Smoking has been inconsistently associated with the prevalence and elimination of cervical HPV[10,11,13].

2. Materials and Methods

This study was a part of Program of Support for Clinical Investigation of the School of Dentistry of the University of Buenos Aires, Argentina. This project was approved by the Institutional Ethics Committee at the School of Dentistry of the University of Buenos Aires in 2017 Resolution (CD) N°628.

A cross-sectional study was conducted from July 2017 to July 2019, including female patients who were over 18 years old with clinical lesions suggestive of HPV infection in the oral cavity who attended the Department of Oral Medicine of the School of Dentistry of the University of Buenos Aires, Argentina. Exfoliative cytology of oral lesions and genotyping of HPV by PCR were performed.

The patients were then referred to the Department of Lower Genital Tract of the José de San Martin Clinic Hospital, for the detection of lesions infected with HPV in genital tract by colposcopy and performing exfoliative cytology and PCR.

The patients answered a survey, through which information on age, occupation, level of education, number of sexual partners, number of sexual partners in the last year, tobacco use, oral sexual practices, contraceptive method used and history of other infections (HIV, HPV) were collected.

Inclusion criteria

For the oral examination, we included women who presented stomatological lesions compatible with HPV infection such as bright white spot, keratosis, verrucosity, microverrucosity, vegetation and microvegetation in the oral cavity.

Exfoliative cytology was performed on those lesions

The smears were placed on a slide, fixed with aerosol lacquer and colored with Papanicolaou technique, then they were observed with an optical microscope with a 40 x objective whose diameter of the visual field was 0.45 mm for morphological and cytological analysis, analyzing the presence or absence of coil cells, presence of bacterial, fungal colonies, inflammatory cells, amphophilia, nuclear alterations in epithelial cells with meander technique from left to right respectively.

In addition, this study was complemented by swabbing the lesions present in the oral mucosa with a brush (cytobrush ®) and placed in a previously labeled Falcon tube, containing sterile physiological solution (0.9% NaCl) which was preserved at 4 ° C until processing within 12 hours of taking the sample to analyze the sample by PCR (polymerase Chain Reaction) with the method of Nested PCR and sequencing.

The samples were incubated with 200 ul of lysis buffer (Lysis tissue buffer, Roche) and 20 ul of proteinase K in agitation at 650 RPM in a thermostatic bath for 12 hours. Subsequently, the extraction of DNA from this lysate was carried out in an automated manner with the MagnaPure 96 equipment (Roche) according to the manufacturer's instructions. To estimate the integrity of the DNA obtained and the absence of PCR inhibitors, a gene fragment of the constitutive gene of β-globin was amplified in all the samples studied, with the universal oligonucleotides BG1 / BG2 (11) by the real-time PCR technique in the LightCycler ® device 2.0 Real-Time PCR System (Roche). The samples where amplification of β-globin was obtained were subjected to viral DNA detection by PCR (primary PCR), using the universal oligonucleotides MY09 / MY11 which amplify a fragment of 450 bp in the conserved region of the L1 gene of HPV (12). In order to increase sensitivity, all samples that were negative for amplification with MY09 / MY11 were subjected to a second amplification (secondary PCR) with universal oligonucleotides (GP5 / GP6), located within the sequence recognized by the oligonucleotides MY09 / MY11 and that amplify a fragment of 150 bp. (13,14). Both PCR reactions were performed on a Veriti® Thermal Cycler (Thermo Fisher Scientific). As a positive control, a detectable sample of HPV type 16 was used and as a negative control we used a negative sample for HPV. The amplification products were visualized on a 2% agarose gel with transilluminator. Capillary electrophoresis of the amplification products resulting from the first and second reaction of PCR was performed, with a previous sequence reaction with the GP5 + / GP6 + primers, in the ABI® sequencer 3500 Genetic Analyzer (Applied Biosystems). Sequence alignments were performed against the reference HPV L1 gene sequences stored in the GenBank database, by BLAST analysis for the final validation of the HPV genotype.

The samples of the oral mucosa were treated following the same indications of the manufacturer for cervical samples.
Besides performing the above protocol, biopsies and susequent pathology studies were made to all the patients who presented potentially malignant oral lesions for its diagnosis.

After this protocol was performed, all patients were referred to the Department of Lower Genital Tract of the "José de San Martín" Hospital of the University of Buenos Aires, Argentina, to assess whether they had cervical lesions through colposcopy observation. The HPV-compatible lesions found were classified as: HSIL (high-grade squamous intraepithelial lesion), LSIL (low-grade squamous intraepithelial lesion), in vagina, VaIN (vaginal intrepithelial neoplasia). They underwent exfoliative cytology, which were placed on slides fixed with aerosol lacquer and colored with Pap smear, and were observed with an optical microscope with a 40 x objective whose diameter of the visual field was 0.45 mm, for cytological morphological analysis by analyzing the presence of coil cells, using the meander technique from left to right respectively.

The instrument for recording qualitative and quantitative data consisted of a form, whose storage method was computerized.

The statistical treatment of the data obtained was performed with the statistical package SPSS statistics 22 correlation coefficient, regression analysis and relative risk were studied.

3. Results

3.1Whole sample (n=76)

76 patients who attended the Department of Oral Medicine of the School of Dentistry of the University of Buenos Aires were examined in which oral lesions compatible with HPV infection were observed, all the patients underwent exfoliative cytology and nested PCR.

The age of the patients were between 23 and 93 years, with an average of 55, a median of 56 and a mode of 52.

In regards to the educational level, 50% of the patients (n = 38) had full secondary education, 39% (n = 30) were university students and 11% (n = 8) had only attended primary school.

Of the total sample, 23.9% (n = 18) of the patients were students, while 41.3% (n = 31) were employees, 13% (n = 10) had a university degree, 2 , 2% (n = 2) were engaged in sex work, 17.4% (n = 13) were housewives and 2.2% (n = 2) were retired.

Regarding the number of pregnancies, 54.3% (n = 42) patients had not had any, 6.5% (n = 5) patients had been pregnant once, 13% (n = 10) patients had had two pregnancies, 17.4% (n = 13) patients had been pregnant 3 times, 4.3% (n = 3) patients had had 4 pregnancies and 4.3% (n = 3) patients had had 8 pregnancies.

The questionnaire showed that the number of sexual partners since the beginning of sexual intercourse was 1 couple in 17.9% of patients (n = 13), two couples in 8.7% of patients (n = 6). 3 sexual partners in 15.2% of patients (n = 12), 4 sexual partners in 19.6% of patients (n = 15), five sexual partners in 4.3% of patients (n = 3), 6 sex partners 8.7% (n = 6), 4.3% had 7 sex partners (n = 3), 2.2% (n = 2) had 9 sex partners, 15.2% (n = 12) had had 10 sexual partners since the beginning of sexual intercourse, 2.2% of the patients (n = 2) had had 20 sexual partners and 2.2% (n = 2) had had more than 50 partners sexual since the beginning of sexual intercourse.

When asked about the number of sexual partners in the last year, 69.6% of the patients (n = 53) responded that they had had only one sexual partner in the last year, 6.5% (n = 5) replied that they hadn't have sexual relationships in that year. 8.7% (n = 6) had had two sexual partners in the last year, while 10.9% (n = 8) had had three. 2.2% of the patients (n = 2) had 6 sex partners and 2.6% (n = 2) had more than 50 partners in the last year.

30.8% (n = 23) did not perform oral sex, while 61.5% (n = 47) performed it without using a condom, only 7.7% (n = 6) of the patients surveyed performed it with barrier method.

In regards to their current contraceptive method, 32.6% (n = 24) of the surveyed patients used a condom, 32.6% (n = 24) of the patients did not use a contraceptive method, 26.1% (n = 21) used Oral contraceptives, 6.5% (n = 5) had fallopian tube ligation and 2.2% (n = 2) used an intrauterine device (IUD).

Of the total number of patients (n = 76), 76.1% (n = 58) had no history of previous genital HPV, while 23.9% (n = 18) had already had a previous infection with the virus .
While 97.4% (n = 74) were HIV negative, 2.6% (n = 2) were HIV positive.

With respect to tobacco use, 78.3% (n = 60) of the patients did not smoke, on the contrary 21.7% (n = 16) did smoke.
Of the 76 patients with oral lesions studied by nested PCR, 51% (n = 39) of them were positive for HPV, and 49% (n = 37) negative for the virus.

Regarding the location of the lesions, it was found that 39.5% (n = 30) were located in the gum, 26.3% (n = 20) in the tongue, 18.4% (n = 14) were located in the palate , 7.9% (n = 6) in buccal mucosa, 3.9% (n = 3) in labial mucosa and 3.9% (n = 3) in floor of mouth.

Regarding the oral lesions identified, the verrucosity was found more frequently in the studied patients 36.8% (n = 28), then in 18.4% of the patients were found keratosis (n = 14) and 18.4% (n = 14) vegetations, white spot 14.5% (n = 11) and tumor 11.8% (n = 9).

The appearance of the lesions was bright white 59.2% (n = 45), opaque white 14.5% (n = 11) and pink 26.3% (n = 20).

Table 1: Sample Characteristics.

Variable	*Statistic*
Age (years)	55 (23-93)
Educational Level	50% Secondary School
Occupation	41,3% Employee
Pregnancies	54,3% None
N° of sexual partners since the beginning of the sexual intercourse	19,6% (4 partners)
N° of sexual partners in the last year	69,6% 1 partner
Unprotected oral sex	61,5%
Condom Use	32,6%
Previous HPV infection	23,9%
HIV	2,6%
Tobacco Use	21,7%

3.2. Analysis of the oral HPV positive sample

With respect to the educational level of patients with oral HPV, 50% of the patients (n = 19) had full secondary education, 39% (n = 15) were university students and 11% (n = 5) had only attended primary school. Of the total sample, 23% (n = 9) of the patients were students, while 41% (n = 15) were employees, 13% (n = 6) were university professionals, 3% (n = 1) was engaged in sex work, 17% (n = 7) were housewives and 3% (n = 1) were retired.
Regarding the number of pregnancies, 21 patients had not had any, 3 patients had been pregnant once, 6 patients had had two pregnancies, 6 patients had taken 3 pregnancies, 1

patient had had 4 pregnancies and 2 patients had taken 8 pregnancies .

The questionnaire showed that the number of sexual partners since the beginning of sexual intercourse was 1 couple in 17.9% of patients (n = 7), two couples in 10.3% of patients (n = 4). 3 sexual partners in 12.8% of patients (n = 5), 4 sexual partners in 20.5% of patients (n = 8), five sexual partners in 5.1% of patients (n = 2), 6 sex partners 7.7% (n = 3), 5.1% had 7 sex partners (n = 2), 2.6% (n = 1) had 9 sex partners, 12.8% (n = 5) had had 10 sexual partners since the beginning of sexual intercourse, 2.6% of the patients (n = 1) had had 20 sexual partners and 2.6% (n = 1) had had more than 50 partners sexual since the beginning of sexual intercourse.

When asked about the number of sexual partners in the last year, 66.7% of the patients (n = 26) replied that they had had only one sexual partner in the last year, 7.7% (n = 3) replied that they hadn't had sexual relationships that year. 10.3% (n = 4) had had two sexual partners in the last year, while 10.3% had had three. 2.6% of the patients (n = 1) had had 6 sexual partners and 2.6% (n = 1) had had more than 50 partners in the last year.

92.3% (n = 36) of the patients performed oral sex without protection, only 7.7% (n = 3) of the patients surveyed performed it with a barrier method.

Regarding their current contraceptive method, 33.3% (n = 13) of the patients surveyed used a condom, 33.3% (n = 13) of the patients did not use a contraceptive method, 25.6% (n = 10) used Oral contraceptives, 5.1% (n = 2) had fallopian tubes linked and 2.6% (n = 1) used a intrauterine device (IUD).

Of the total of patients with oral HPV (n = 39), 82.1% (n = 32) had no history of prior genital HPV, while 17.9% (n = 7) had already had a previous infection with the virus. While 97.4% (n = 38) were HIV negative, while 2.6% (n = 1) were HIV positive.

With respect to tobacco use, 84.6% (n = 33) of the patients studied did not smoke, on the contrary 15.4% (n = 6) did smoke.

Among the 39 positive HPV lesions it was found that the most frequent location was gum 31% (n = 12), tongue 23% (n = 9), palate 23% (n = 9), buccal mucosa 15% (n = 6), 3% labial mucosa (n = 1) floor of mouth 5% (n = 2). Table 2.

Verrucosity was the lesion that was most frequently associated with the presence of the virus, being positive in 46% of the patients studied (n = 18), vegetation 21% (n = 8), keratosis 15% (n = 6), 10% tumor (n = 4) and 8% white spot (n = 3). Table 3

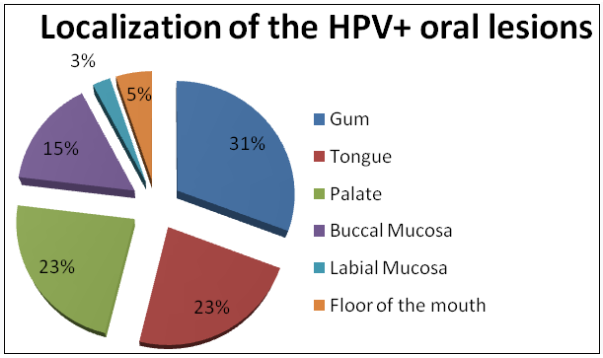

Table 2. Localization of oral lesions positive for HPV.

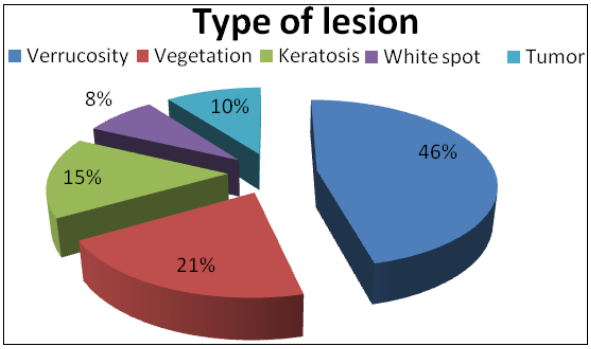

Table 3. Type of lesion HPV +.

Regarding the cytological observation of HPV positive lesions colored with Pap smears, they were extended with a clean background with the presence of fissured degeneration cells (cracked plasma), superficial cells with coil cells, eosinophilic cytoplasmic degeneration (polka dot cell), nuclear duplication, amphophilia. Regarding the cytologies of patients who did not have HPV in the lesions, inflammatory cells, cocci, hyphae of Candida spp., amphophilia and absence of coilocitosis were observed. Regarding their appearance, HPV positive lesions were mostly associated with bright white lesions 67% (n = 26), pink lesions 25% (n = 10) and opaque white lesions 8% (n = 3). (Table 4). The HPV genotypes found in the lesions were HPV16 33.3% (n = 13), HPV35 2.6% (n = 1), HPV58 2.6% (n = 1), HPV2 2.6% (n = 1) HPV33 2.6% (n = 1), HPV13 5.1% (n = 2), HPV11 17.9% (n = 7), HPV26 2.6% (n = 1), HPV6 12.8 % (n = 5), HPV18 7.7% (n = 3), HPV31 2.6% (n = 1), HPV64 5.1% (n = 2) and HPV51 2.6% (n = 1) . (Table 5) The high-risk oncogenic genotype HPV 16 (n = 13) was mostly associated with bright white lesions 77% (n = 10), opaque white lesions 8% (n = 1) and pink lesions 15% (n = 2). All oral lesions associated with this virus genotype were elevated.

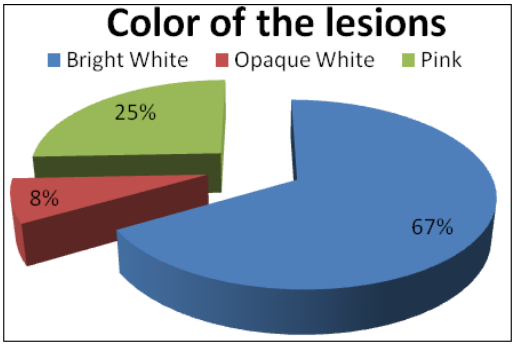

Table 4. Color of the oral lesions.

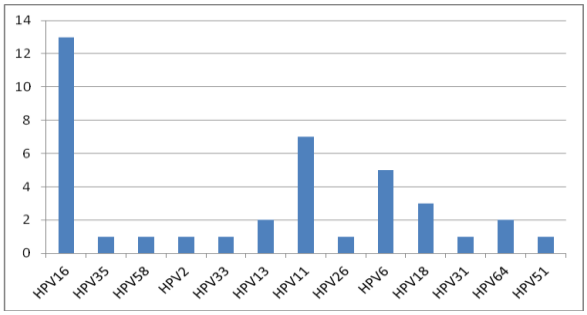

Table 5. Types of HPV found in oral lesions

The low-risk genotype HPV 11, was associated with bright white lesions 85.7% (n = 6) and opaque white lesions 14.3% (n = 1) . Regarding the thickness of the lesions, this viral genotype was more frequently present in flat lesions.
Regarding the presence of the virus in elevated lesions vs flat lesions, the OR 3.31 95% CI (0.80-13.61) was estimated.

Taking into account the presence of the virus in bright white vs. opaque white lesions, the OR 3.64 95% CI (0.85-15.6) was estimated.

The regression coefficient for positive / negative oral HPV and occupation, level of studies, number of sexual partners since the beginning of sexual intercourse, use of barrier method for oral sexual intercourse was estimated, being significant for the latter (B = 1.030) 95% CI (0.363-21.67).
The regression coefficient for positive / negative HPV and smoking habit (B = 1,038) 95% CI (0.668-11.943) was estimated.

We found a positive correlation between smoking habits and unprotected oral relationships with the presence of the HPV virus.

The presence of human papillomavirus was detected in potentially malignant oral lesions. Six lesions co-infected with HPV were found, four of which had high-risk oncogenic HPV genotypes. Table 6.

Table 6: Potentially malignant lesions related to HPV genotypes.

Potentially malignant lesions	*HPV Genotype*	*Number of cases*
Oral Lichen	6-11-58	3
Leukoplakia	16	1
Oral proliferative verrucous leukoplakia	16	2

3.3. Analysis of the gynecological positive HPV sample

Of the 76 patients examined in the TGI department, 11 had lesions in the lower genital tract. These were examined by colposcopy, Pap tests and also specific genotype PCR.

Ten gynecological samples were HPV positive. The HPV genotypes found were: 6 (n = 2), 11 (n = 1), 16 (n = 3), 33 (n = 1), 56 (n = 1) 62 (n = 1) and 66 (n = 1).
Regarding the lesions associated with the virus, 4 LSIL, 5 HSIL and 1 neoplasm were found.

In 3 cases (27.27%) there was coinfection with genital and oral HPV, in two patients the genotypes of HPV 11 and 16 were coincident in both mouth and genitals, while in one case the virus genotypes found were different (Oral : HPV 26 and Genital: HPV 33). (Table 7, Table 8)

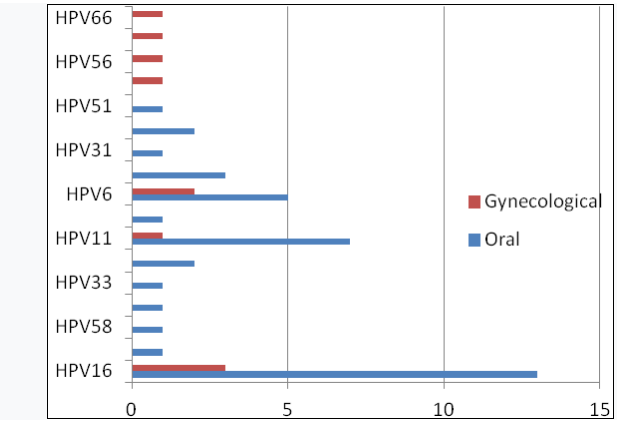

Table 7: Oral and genital HPV genotypes found.

Table 8: HPV genotypes found in oral and genital samples

Patient	*Oral*	*Genital*
1	Not detectable	62
2	Not detectable	6
3	Not detectable	16
4	Not detectable	56
5	11	11
6	Not detectable	16
7	26	33
8	Not detectable	66
9	Not detectable	Not detectable
10	16	16
11	Not detectable	6

4. Conclusions

In this study, 76 patients presented oral lesions suggestive of HPV infection, which made up the total sample. In only 39 the presence of the virus could be confirmed. Only 11 patients had lower genital tract lesions suggestive of HPV infection, of which 10 were positive for the virus. In 2 of the cases the HPV genotypes found in both oral and genital mucosa matched (HPV 16 and HPV 11, respectively), while in one sample the genotypes detected in both mucous membranes did not match (HPV 26 in oral mucosa and HPV 33 in genital mucosa).

In this study, the percentage of genital oral HPV coinfection was 27.27%. This suggests that oral HPV is not a predisposing factor for genital HPV infection in the same patient.

The oral location where the lesions were most frequently located in this study was the gum in 31% of the samples (n = 12), then in the same percentage the lesions were located in the tongue and palate 23% (n = 9).

The HPV genotype of high oncogenic risk 16 was found mostly associated with bright (translucent) white lesions.

Verrucosity was the lesion that was most frequently associated with the presence of the virus, being positive in 46% of the studied patients (n = 18).

The morphological cytological findings in the HPV positive patients were: presence of coilocitic cells, presence of fissured degeneration cells (cracked plasma), eosinophilic cytoplasmic degeneration (polka dot cell), nuclear duplication and amphophilia.

Within the positive sample for oral HPV, according to the questionnaire, it could be concluded that with respect to the number of sexual partners who had had in the last year 66.7% of the patients had only one partner, 61, 5% maintained unprotected oral sex, 33.3% used the condom as a contraceptive method, 82.1% of the sample had no previous history of genital HPV, 84.6% was not associated with smoking habit, 41% were employees, 50% had full secondary education and 53.8% of the patients had not been pregnant.

A positive correlation was found between unprotected oral relationships with the presence of the oral HPV virus. In reference to the relationship between tobacco consumption and oral HPV infection, there is a positive correlation between HPV infection and smoking habits.

Another remarkable finding in this work was the detection of the presence of human papillomavirus in potentially malignant oral lesions. Six potentially malignant lesions co-infected with HPV were found, four of which had high oncogenic risk HPV genotypes.

5. Discussion

In this work, the presence of HPV in the oral mucosa and lower genital tract of women with a clinical oral diagnosis of lesions suggestive of viral infection was evaluated.

It has been pointed out that this type of study is important to determine risk factors related to the incidence and persistence of this infection, as well as to establish transmission and control mechanisms [1]. The results show that the presence of HPV was greater in the oral mucosa than in the lower genital tract, there is no coincidence with the world literature since this study was conducted in a center specialized in the observation of oral mucosa. It has been suggested that this difference between both anatomical regions may be due to characteristics of the oral mucosa that the cervical mucosa does not share, including keratinized tissue that would act as a barrier against microbial infections, making it difficult for the virus to enter the basal cell layer. In addition, saliva contains antimicrobial agents such as IgA, cytokines, lactoferrin and lysozyme whose production increases during infectious processes.

These agents also protect against HPV[2,3,4] infection. However, other researchers consider that the difference in the frequency of HPV detected in the oral and genital mucous membranes suggests that genital infection is not necessarily a predisposing factor for oral infection in the same patient and that this can be considered an independent event[5]. Carcinogens dissolved in saliva such as alcohol or cigarettes provide opportunities for the harmful activity of the virus. According to the world literature, the sites most frequently affected by the appearance of the virus are the lips, the palate, the tongue, the Gum, uvula, tonsils and floor of mouth[6,7,16], according to our study the first place corresponds to the gum followed by tongue and palate.

Other aspect to consider regarding the differences in the detection of HPV in the mouth and cervix is the variation in the susceptibility to HPV infection and / or viral tropism, as well as the ability to resolve the infection in both regions, which It can occur independently or at different intervals [8].

The mode of transmission of the virus is still controversial, factors such as the susceptibility of the host and its immune level must also be considered.

The results obtained through this study would suggest that oral-genital HPV coinfection does not occur frequently since the virus would exhibit a different biological behavior in both mucous membranes, and they would have different mechanisms to resolve the infection.

The prevalence rate of HPV in oral mucosa varies according to the techniques of sample collection, detection methods, level of sensitivity, primers used to perform the PCR and its inhibitors present in the samples [9,10,11,12].

In the literature the increase in the number of sexual partners is taken as a risk factor for oral and / or genital HPV infection [13, 14, 15], but in our study the number of sexual partners does not seem to increase the risk of it.

The results obtained in this study suggest that HPV infection in the oral cavity and TGI, have a different biological behavior, which would influence the ability to neutralize the viral infection differently in each epithelium, there being a viral tropism or preference for a certain type of location (genital / oral) [17].

It is important to highlight the importance of HPV detection in the mouth for infection control in sexually active populations with genital infection.

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