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Histopathological Findings of Cervical Biopsy in Patients with Positive Human Papillomavirus (HPV)PCR

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Abstract

Background: The human papillomavirus is currently one of the most important risk factors of cervical cancer, which is one of the three most frequent malignancies in women globally. As a result, this study aims to examine the histopathology of cervical biopsies in individuals who had a positive HPV PCR titer.

Methods: In this cross-sectional study, we initially collected the data from the patients' records referred to Shahid Motahari Hospital's oncology clinic in 1995 and 1996, which included the variables CNI1,2, and 3, age, marital status, and type of contraception used. Then, while recording the histopathological information of cervical biopsies in patients with a positive HPV PCR titer, we classified the patients into low-risk and high-risk groups based on the type of HPV that they were infected with and investigated its association with the factors evaluated.

Results: The results of our study showed that with increasing the marriage age and duration the infection with high-risk types of HPV was higher in the subjects. Furthermore, ASCU was reported in 21 (35.6%) patients, LSIL lesions in 7 (11.9%) cases, and HSIL lesions in 2 cases (3.4%).

Conclusion: Our findings demonstrated the diversity of multiple HPV species in the examined samples, as well as their relationship to the factors evaluated. hence, there is a strong need to investigate the incidence of Pap smear pathologies in a larger statistical sample in order to provide a more realistic and critical picture of the virus epidemiology in Iranian society. In future studies, it is also crucial to evaluate other characteristics such as couples' sexuality and education degree.

Keyword: Human Papillomavirus; PCR; Pap smear; Cervix cancer

Introduction

Papillomaviruses (PVs) are a small group of viruses that have double-stranded DNA and are members of the papillomavirus family [1,2]. human papillomavirus (HPV) is the most common sexually transmitted illness , that infects over 80% of women over the age of 50 in the United States [3]. More than 85 strains of HPV have been discovered so far, with at least 35 of them being detected in female genital infections [4]. Cohort studies have revealed that HPV DNA is required for cervical neoplasms growth, and its elimination predicts neoplastic cell regression [5-7]. Women who have HPV DNA but no cervical legions are at a higher risk of Squamous Intraepithelial Lesion (SIL) progression [8].

Based on the relative risk of developing high-grade legions and invasive malignancies, HPV viruses are classed as high-risk (HPVs 16, 18, 45, 56), medium-risk (HPVs31,33,35,51,52,58), and low-

risk (HPVs 6,11,42,43,44) [9-11]. Cervical cancer has been linked directly to HPV, with a portion of the viral genome (E proteins) causing malignant cell transformation, chromosomal changes in cervical epithelial cells, and the development of cervical cancer [12].

Following the development of a primer for HPV detection by polymerase chain reaction (PCR), it was shown that HPV plays a significant role in cervical cancer, since virtually all the samples contained HPV DNA [13, 14]. However, since the majority of precancerous lesions arise in the squamous epithelium or metaplastic endocervical epithelium, the identification of HPV DNA in Low grade squamous inthraepithelial lesion (LSIL) and High grade squamous inthraepithelial lesion (HSIL) lesions inside the squamous epithelium has grown to 80-90 % with the advancement of HPV detection technologies [13,15].

Overall, the community and at-risk populations need early and prompt identification and treatment of human papilloma infections using cost-effective and accurate technologies such as PCR. Therefore, the purpose of this study is to look at the histopathology of cervical biopsies from patients with positive HPV PCR titer. In which we were able to take a step toward a more accurate understanding of this illness in the Iranian community.

Methods

Study Overview

In this cross-sectional study, the histopathological changes of cervical biopsies were investigated in 59 patients that were referred to Shahid Motahari Hospital's cancer clinic between 2016 and 2017 who had a history of HPV infection verified by PCR and underwent biopsy. Data were collected using a researcher-designed checklist that includes CNI 1, 2, and 3, as well as age, marital status, and contraceptive method usage. In this study, we assessed patients with HPV history that was confirmed by PCR and excluded the patients' records that lack of information due to any reason and we were unable to update the record after a phone call. In this study, we classified the patients based on the type of HPV that they were infected with . As a result, patients who tested positive for HPV 16, 18, 45, and 56 were assigned to group I (the high-risk group), while patients who tested positive for HPV in the moderate and low-risk groups were assigned to the other group (the group II).

Statistical Analysis

In this study, the t-test or its non-parametric equivalent was used to compare quantitative data, while qualitative data was compared using the Chi-square test and, if appropriate, the Fisher test. In all instances, the significance level was less than 0.05.

Results

Basic Information

According to our study's findings , the mean and standard participants' age deviation was 38.30 8.78 years, with a range of 21-52 years. This study's participants were all married. In our study , ten patients (16.94%) were remarried. In our study, the mean and standard deviation of marital length was 15.16 7.33 years with a range of 6-29 years. In our study, 36 cases (61%) used combined oral contraceptive pills and 14 cases (23.7%) used intermittent method, 8 cases (13.6%) used condoms and one case used ampules for contraception. In our study, 23 cases (39%) were in the high-risk group for HPV (group I), and 36 patients (61%) were in the lower-risk groups for HPV (group II).

Histopathological Findings

In our study , 9 individuals had CIN1, 2 had CIN2, 2 had CIN3, and the others were normal. There was a significant relationship between patient pathology and HPV type (groups I & II) ($p = 0.002$). So that, CIN was found in 11 out of 33 people in Group I, while only two out of 36 people in Group II had CIN1. Similarly, a significant difference was observed between the mean age and the two classified HPV groups (45.47. 5.83 vs. 33.72 ± 7.14, $p = 0.001$), which showed that the mean age was higher in group I. The mean marriage duration was significantly different in both groups therefore it was about 6 years longer in group I (18.56 ± 7.12 vs. 13.02. 6.70, $p = 0.04$). There was no significant difference ($p = 0.629$) between the contraceptive methods used by patients and the two HPV groups. Furthermore, the findings of our study revealed that the rate of ASCUS in the patients analyzed was 21 cases (35.6%), which had a significant association ($P = 0.001$) with the study's groups. Furthermore, 9 cases of LSIL lesions were detected in our samples, with 7 cases in the high-risk group and 2 cases in the low-risk group, which were statistically significant ($P = 0.027$) with each other. HSIL lesions were seen in two individuals (3.4%) in our cases, one in the high-risk group and one in the low-risk group.

Discussion

The epidemiology of HPV positive cases in our study was effectively described by taking into account the histological status and pathology of the examined patients at Shahid Motahari Hospital in Urmia. In this respect, in our study HPV positive patients were divided into high-risk and low-risk groups, in which had a significant relationship with the type of pathology the patient infected with, the patient's histology (squamous lesions and LSIT), and the patient's age. These findings may point to a greater emphasis on high-risk disease categories and, as a consequence, improve illness management.

In literature, the average age of cervical cancer onset is 50-52 years [16,17],which is older than the average age of our study's patients (38 years). The target population might be responsible for the older average age of patients in this evidence. Therefore our study's patient were infected with human papillomavirus rather than cervical cancer, hence, in fact they were a population at risk for cervical cancer. Several researchers have examined the patients' marital status and the number of their sexual partners

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[18,19]. In all investigations, having several sexual partners was shown as a risk factor for cervical cancer [20,21]. According to our findings, the average length of marriage duration in the patients with higher-risk papilloma is much longer than in patients with high-risk papilloma virus. In addition, it's necessary to mention that almost 17% of the patients in our study were remarried. In a study done by Monroe et al. [22], women who had used OCP for less than 5 years were not at higher risk cervical cancer group, but this risk was observed after taking these pills for more than 5 years. Moreover, in another evidence, taking the OCP for more than 6 years was listed as a cancer risk factor [20]. Therefore, approximately 61 percent of the individuals in our study utilized OCP. However, no statistically significant link was found between the usage of contraceptive methods and the low-risk and high-risk HPV groupings. Having unprotected intercourse with an HPV-infected individual, has been demonstrated in earlier researches [23,24] to be a main risk factor for cervical cancer. According to Nojomi et al. [16], around 75% of patients with cervical cancer had never used a condom. As a result, the absence of a meaningful association in our study can be attributed to the study's small sample size. It is essential that in future studies , a larger statistical population will be chosen, and the patients' spouses' sexual function would be assessed.

In our investigation, ASCU was reported in 21 (35.6%) patients, LSIL lesions in 7 (11.9%) cases, and HSIL lesions in 2 cases (3.4%). In this respect, the frequency of ASCUS, LSIL, and HSIL in a study done by Condyle et al. [25] with the same purpose was comparable to our study, while the rate of AGUS in this study was reported to be 7.3 %, which was not reported in our study , it can be due to the insufficiency of the Pap smear method in this study, as well as the lower incidence of AGUS in our study region, which deserves more examination.

Conclusion

Overall, the findings of our study suggest that it is necessary to pay more attention to the high-risk types of the disease and, as a consequence, improve the disease management. More researches in various sections of the population seems to be critically important in this respect. More specific information may be acquired to describe the differences between groups more clearly.

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