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## **The effect of being diagnosed with human papillomavirus infection on women's sexual lives**

### **Materials and Methods**

The present prospective observational study was conducted with women referred to our gynecology outpatient clinic upon being diagnosed with an HPV infection by the community based cervical cancer screening program. After obtaining the ethical approval (approval number: 2017/33) from our hospital's local ethics committee, the patients who had been diagnosed with a high-risk HPV (HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 69, and 82) infection for the first time in their lives and who were sexually active and in the reproductive period were included in this study. All the patients were  $\geq 30$  years old (cervical cancer screening with co-test starts at the age of 30 years in Turkey).

Post-menopausal women, and patients with the low-risk HPV genotypes (HPV 6 or 11), sexual penetration disorders, chronic systemic diseases, a sexual abuse history, or a prior HPV infection, and those under any antidepressant medication or diagnosed with psychiatric disorders were excluded from the study. Additionally, patients who did not agree to participate in the study after reading the informed consent form and those who did not come for the follow-up visit were also excluded.

The patients who met the inclusion criteria were informed about the details of the study and were asked whether they would have liked to participate in this study. Written informed consent was obtained from all the patients who agreed to do so. The sociodemographic data of these patients, such as pregnancy, parity, Body Mass Index (BMI), educational level, and marital status were recorded. We had the participants filled out the FSFI and BAI questionnaires at the first visit to assess the initial sexual functions and anxiety levels of the women. Then the participants were informed about their co-test results and were divided into four groups according to their HPV genotypes and cytology results as follows: Group 1, HPV 16/18-positive and normal cytology; Group 2, HPV 16/18-positive and abnormal cytology; Group 3, non-16/18 HPV-positive and abnormal cytology; and Group 4, non-16/18 HPV-positive and normal cytology.

The detailed information, including the sexually transmitted nature, occurrence rate, and progress of the disease, as well as the relationship between high- vs. low-risk HPV types and the development of CIN or cervical cancer were explained to the participants by a clinical

expert. After all the participants had undergone a routine gynecologic examination, they were informed about the treatment and follow-up plans. The management of the patients with abnormal co-test results was planned according to the American Society for Colposcopy and Cervical Pathology (ASCCP) guidelines.<sup>21</sup> All of the patients were called in two months later for a follow-up to assess the changes in their anxiety levels and sexual functions by using the FSFI and BAI questionnaires. The patients in groups 1, 2, and 3 were directly referred to colposcopy per ASCCP guidelines, and the patients in group 4 were referred to colposcopy upon their gynecologist's suspicion of a cervical lesion. All of the patients were informed about the colposcopy procedure at their first visits, and colposcopy was performed on the patients at their second visits.

### **Cervical Cancer Screening and the Management Strategy**

According to the Turkish national cervical cancer screening program, the initial cervical screening test is recommended at the age of 21 years, and women < 30 years old are screened with the Papanicolaou (PAP) test alone every three years. Women  $\geq$  30 years old are screened with co-testing (HPV testing alongside liquid-based cervical cytology) every five years. If HPV test results are positive, then HPV genotyping is performed, and the PAP test is cytologically evaluated. If HPV test results are negative, then the PAP test is not evaluated. Patients with HPV 16/18 (regardless of the cytology status) or those infected with HPV strains other than 16/18 (non-16/18 HPV-positive) and exhibit abnormal cervical cytology are referred to a specialist for colposcopy. For non-16/18 HPV-positive patients who exhibit normal cervical cytology, an additional co-test is recommended 1 year after the index test. However, if the gynecologist has a clinical suspicion of a cervical lesion, these patients may also be referred for colposcopy.

### **HPV Diagnosis and Genotyping:**

In Turkey, HPV testing for cervical cancer screening is performed at primary level healthcare centers, such as KETEM (Kanser Erken Teşhis, Tarama ve Eğitim Merkezi; Cancer Early Diagnosis, Screening and Educational Centers). Two cervical swab samples are taken from the patients. The first sample is collected and smeared onto a glass slide for cytological analysis. The second sample is collected with a different brush, and the tip of the brush is broken and then placed into a 5-ml Standard Transport Medium (STM) for HPV DNA analysis. Samples across the country are delivered into two national laboratories for the cervical cancer screening program. In these laboratories, the Hybrid Capture 2 (Qiagen, Germany) system is used for HPV DNA analysis. This system detects 13 different high-risk HPV genotypes (HPV16, 18,

31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and 68) and reports the results as positive or negative. HPV-DNA–positive samples are genotyped with the CLART® kit (Genomica, Madrid, Spain). The results about HPV status, HPV genotype, and cytology (when HPV-positive) are recorded into a National Screening software system and sent to the patient's family physician/nurse at primary healthcare centers.

### **Beck Anxiety Inventory**

The BAI questionnaire consists of 21 questions and is a brief assessment of anxiety with an emphasis on somatic symptoms. It was developed to measure anxiety and depression levels, and the inventory has been validated for the Turkish population.<sup>20, 24</sup> Participants indicate how much they have been bothered by each symptom over the past week. Responses are rated on a 4-point Likert scale, and range from 0 (not at all) to 3 (severely). Total score is calculated by summing the rates from the 21 questions. It is classified as follows: a score of 0–21 = low anxiety, a score of 22–35 = moderate anxiety, a score of  $\geq 36$  = potentially concerning levels of anxiety.

### **Female Sexual Function Index**

Sexual dysfunction was assessed via a self-administered FSFI questionnaire which had been adapted to the Turkish population by Aygin et al.<sup>19, 25</sup> This is a 19-item questionnaire that contains the following six domains: desire, arousal, lubrication, orgasm, satisfaction, and pain. The scores are ranked from 0–5 for the arousal, lubrication, orgasm, and pain domains; and 1–5 for the satisfaction and desire domains. Domain scores were obtained by summing the rates from the questions in each domain and then multiplying them with the following domain factors: 0.6 for desire, 0.3 for arousal and lubrication, and 0.4 for orgasm, satisfaction, and pain. The total score was obtained by summing the six domain scores. The FSFI scores ranged from 2.0 to 36.0, with higher scores indicating better sexual function and categorized into four groups: normal sexual function (total FSFI score  $\geq 26.55$ ), mild risk for a female sexual disorder (FSD) (total FSFI score 18–26.55), moderate risk for FSD (total FSFI score 11–17), and severe risk for FSD (total FSFI score  $\leq 10$ ).

### **Statistical Analysis**

Data analysis was performed by using SPSS (IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.). A one-sample Kolmogorov–Smirnov test was performed to analyze the distribution of the clinical variables. The frequencies and percentages of the categorical variables and the mean, standard deviation, median, and range values of the continuous and ordinal variables are presented. The study groups were compared using Oneway analysis of variance (ANOVA) and the Kruskal Wallis H tests for the parametric and non-parametric

variables, respectively. The Bonferroni correction was performed for posthoc analyses of the significant differences in the second-visit BAI score among the study groups. The Wilcoxon rank test was used for the comparison of the BAI and FSFI scores at the first and second visits. For all the calculations, a p-value of  $< .05$  was considered statistically significant.