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Article title: Risk factors for the development of anogenital diseases in women of reproductive age

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ABSTRACT

Introduction: Human papilloma virus (HPV) infection is one of the most common sexually transmitted infections in men and women in the world. Human papilloma virus is directly associated with accumulative warts and cervical cancer, the second most common neoplasia among women.

The aim of this study was to assess the risk factors for the development of anogenital diseases in women in reproductive age, with the analysis of accompanying symptoms and comorbidities.

Subjects and research methods: the study included female subjects (n = 100) who are treated at the Clinic of Gynecology and Obstetrics UKCS. The basic division of the patients was based on the presence of condyloma. The research was based on the analysis of relevant data obtained in 100 HPV positive genotypic patients.

Research results: The determined difference in the frequency of postcoital bleeding between the examined groups was significant (p = 0.002). No significant difference in the age of first coitus was found between the examined groups (p = 0.768). A significant difference in the number of sexual partners was found between the examined groups (p = 0.018).

Conclusion: Subjects with the presence of condyloma have statistically significantly more frequent postcoital bleeding, a larger number of partners and somewhat younger have sexual intercourse compared to subjects without the presence of condyloma.

Key words: genital warts, human papilloma virus, cervix

INTRODUCTION

Human papillomavirus (HPV) infection is one of the most common sexually transmitted infections in men and women worldwide. Almost all sexually active people will get at least one HPV infection in their lifetime. Although most HPV infections disappear spontaneously within a few months, they can become permanent with a subsequent increased risk of developing genital warts and certain cancers (1). Human papilloma virus is directly associated with accumulated warts and cervical cancer, the second most common neoplasia among women (2).

Human papillomavirus infections may have clinical manifestations ranging from self-limiting benign growth in the skin and mucosal epithelium to malignant growth. HPV infects basal epithelial cells (non-differentiated keratinocytes) of the squamous-columnar junction, especially the cervix. Although we have a very good understanding of HPV oncogenesis today, we have very powerful methods for diagnosing, treating, and preventing precancerous lesions associated with HPV, however, more than 270,000 women die each year from cervical cancer worldwide (3). Factors that increase the risk of developing cervical cancer are those that increase exposure to HPV infection or facilitate the persistence of HPV, ie. early onset of sexual activity, multiple sexual partners, high parity, low immunocompetence, use of oral contraceptives, and cigarette consumption (4).

Genital warts can manifest as four morphological features: condyloma accumulations, smooth or flat papular lesions, or keratotic warts. Except for the appearance, they are often asymptomatic, except in some cases of vulvar warts that can cause dyspareunia and discomfort, itching, vaginal warts and vaginal discharge, bleeding, obstruction of the birth canal and neonatal infection that can lead to juvenile recurrent papillomatosis, perianal and intraanal warts which cause pain, bleeding during defecation, and itching. Genital warts can have profound effects on patients' quality of life. They may withdraw spontaneously or remain still for long periods of time. They may be resistant to treatment with high recurrence rates leading to significant health care costs (5).

The aim of this study was to assess the risk factors for the development of anogenital diseases in women of reproductive age, with the analysis of accompanying symptoms and comorbidities.

Respondents and research methods

The research is a retrospective, descriptive - analytical, study.

The study included subjects (n = 100) who are treated at the Clinic of Gynecology and Obstetrics UKCS, in the study period of three years 2018-2020. comparative

The research was based on the analysis of relevant data obtained in 100 HPV positive genotypic patients. The following data were monitored: age, onset of sexual activity, education, number of partners, intermenstrual bleeding, postcoital bleeding, vaginal secretions, pelvic pain, presence of comorbidities and high-grade cervical dysplasia.

The basic division of the respondents was based on the presence of genital warts (condyloma).

Statistical analysis of data

The results were processed and analyzed by statistical methods using the computer program SPSS (SPSS-Statistical Package for Social Sciences) computer program for statistical analysis, version 21.0. Results are expressed as absolute numbers and percentages, as average (X) and standard deviation (SD), and as median and interquartile range (25-75 percentile). The Kolmogorov-Smirnov and Shapiro-Wilk tests were used to test the significance of the difference in deviation from the normal distribution. Independent numerical variables were analyzed by t-test for those who met the conditions for application, and the corresponding non-parametric tests (Mann-Whitney U test) for variables in which an incorrect distribution was found. The Hi-square test and the Fisher exact test were used to analyze the category variables. A $p < 0.05$ value was taken as statistically significant.

Results

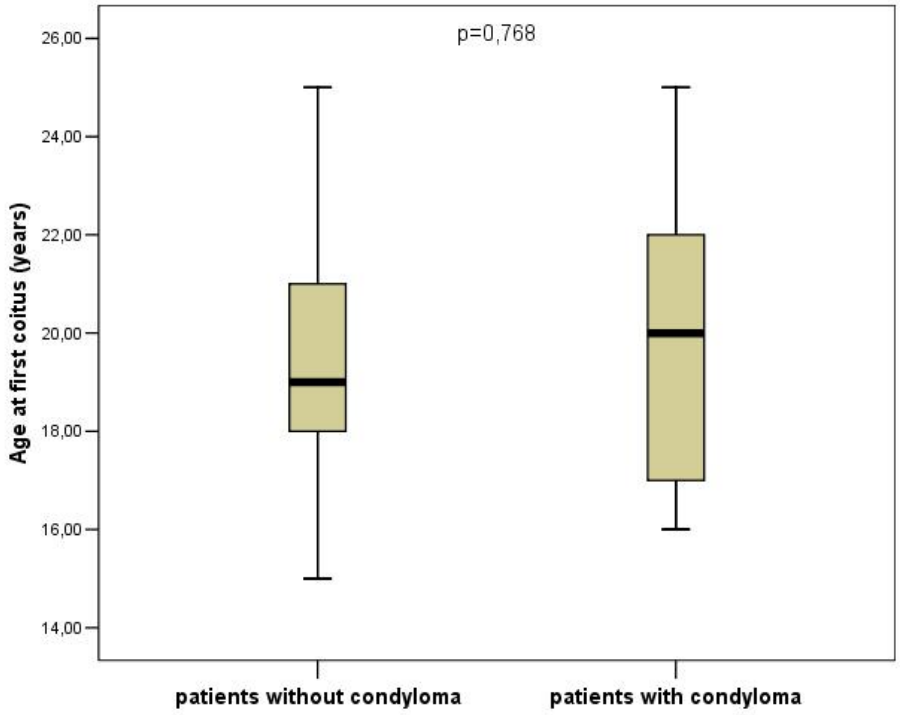
Table 1. Baseline characteristics of the examinees in relation to the presence of condyloma

VARIABLES	Group without condyloma (n=79)	Group with condyloma (n=21)	p
Age	38,69±8,12	35,14±6,85	0,050
Education (SSS / VSS)	50 (63,3%) / 29 (36,7%)	13 (61,9%) / 8 (38,1%)	0,907
Intermenstrual bleeding	12 (15,2%)	4 (19,0%)	0,445
Postcoital bleeding	21 (26,6%)	13 (61,9%)	**0,002**
Vaginal secretion	45 (57,0%)	15 (71,4%)	0,229
Pelvic pain	21 (26.6%)	4 (19,0%)	0,345
Comorbidity present	5 (6,3%)	3 (14,3%)	0,219
CIN (CIN I / CIN II and higher)	16 (20,3%) / 63 (79,7%)	4 (19,0%) / 17 (81,0%)	0,587

Results are expressed as absolute numbers and percentages, as average (X) and standard deviation (SD), CIN-cervical intraepithelial neoplasia, SSS-secondary education, VSS-university education.

Table 1 shows the baseline characteristics of the subjects in relation to the presence of condyloma. The average age of subjects without condyloma was 38.69 ± 8.12, and subjects with condyloma 35.14 ± 6.85, although they were slightly younger, no statistically significant value was found.

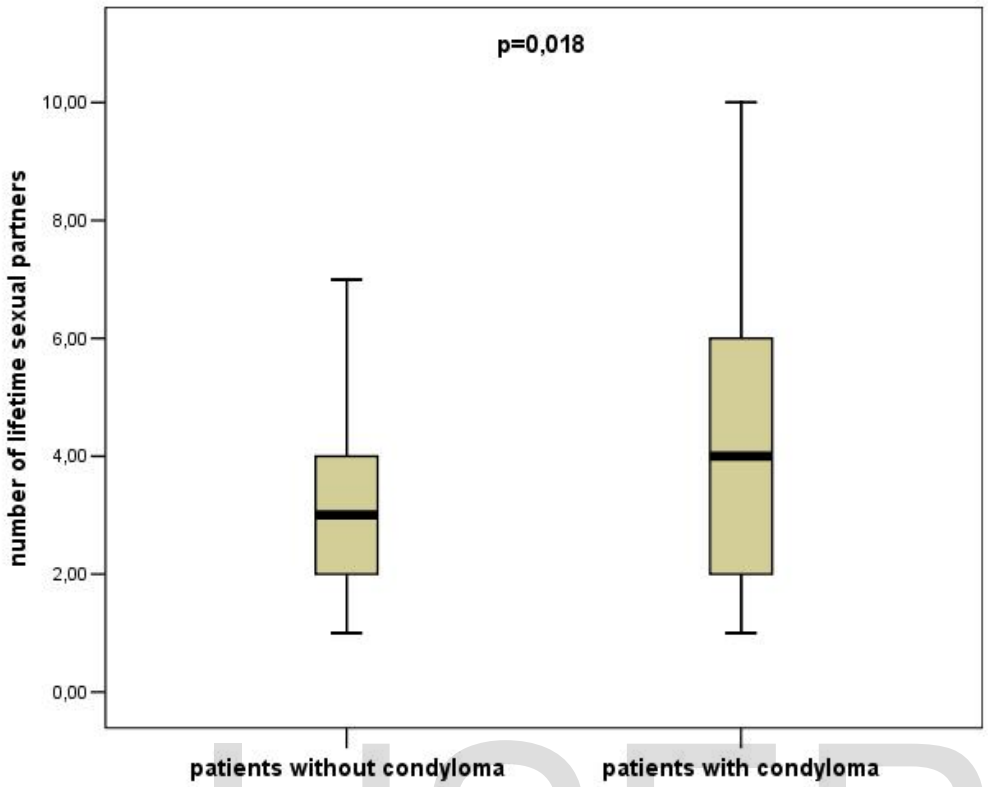
The frequency of postcoital bleeding in the group of subjects with condyloma was 13 (61.9%), in the group of subjects without condyloma 21 (26.6%). The determined difference in the frequency of postcoital bleeding between the examined groups was significant (p = 0.002). Other parameters (education, intermenstrual bleeding, vaginal secretion, pelvic pain, presence of comorbidities, cervical dysplasia) did not differ significantly between the examined groups.



Graph 1. Age at first coitus of the subjects in relation to the presence of condyloma

Results are expressed as median and interquartile range (25-75 percentile)

The age of first coitus in subjects without condyloma was 19.0 (18.0-21.0), while in subjects with condyloma present 20.0 (17.0-22.5). No significant difference in the age of first coitus was found between the examined groups (p = 0.768) (Graph 1).



Graph 2. Number of sexual partners in respondents in relation to the presence of condyloma

Results are expressed as median and interquartile range (25-75 percentile)

The number of sexual partners in women without condyloma was 3.0 (2.0-4.0), while in women with condyloma the number was 4.0 (2.0-6.0). A significant difference in the number of sexual partners was found between the examined groups (p = 0.018) (Graph 2).

DISCUSSION

Genital warts are common manifestations of human papillomavirus (HPV) infection. They are usually associated with HPV6 and HPV11. However, many other types of HPV have also been isolated in genital warts, including HPV 2, 40, 42, 43, and 54. Although there is a growing prevalence and incidence of genital warts in the general population in Europe and the United States, countries such as Australia and England, with a high coverage of HPV vaccination, reported a reduction in the number of genital warts among young women (5).

One of the basic symptoms of the presence of genital warts and precancerous and cancerous lesions on the cervix is certainly postcoital bleeding. There is a separate algorithm for managing bleeding symptoms related to cervical cancer, defined as persistent postcoital bleeding, inexplicable recurrent intermenstrual bleeding, and postmenopausal bleeding. The guidelines advise primary care physicians to investigate symptoms by a combined HPV test and cytology (6).

In this study, it was found that the frequency of postcoital bleeding between the examined groups was significant (p = 0.002). In the group of examinees with condyloma present it was 61.9%, in the group of examinees without condyloma present 26.6%. In a study by Cohen et al. using the large Health Maintenance Organization (HMO) database to identify all women who reported postcoital bleeding between 2012 and 2015, the annual incidence of postcoital bleeding ranged from 400 to 900 per 100,000 women, most among patients aged 26-30 years. Among a sample of 411 cases of postcoital bleeding who underwent colposcopy, 201 (48.9%) had an indicated biopsy. Biopsy results reported 68 cervicitis (33.8%), 61 koilocytosis / CIN 1 / condyloma (30.3%), 44 normal tissues (21.9%), 25 cervical polyps (12.4%), 2 CIN 2 / 3 (1%) and 1 cancer (0.5%). The positive predictive value for coylocytosis / CIN 1 pathology or higher was 15.6% (64/411) and 0.7% for CIN 2 or higher pathology (3/411). Compared with the control group, subjects with postcoital bleeding were significantly (P = 0.04) more likely to develop CIN 1 or higher pathology (OR 1.82, 95% CI 1.02–3.33) (7) .

Tan et al. in their study, wanted to determine the risk of cervical cancer and its precursors in women with recurrent postcoital bleeding, with negative cytology, or co-test. A retrospective analysis was performed in two cohorts of women with postcoital bleeding referred to a tertiary colposcopy clinic. Group (1) (n = 1846) between 1 January 2000 and 31 December 2016 (cytology screening) and group (2) (n = 215) from 1 January 2018 to 31 December 2019 after introduction of primary HPV screening. In 1217 (65.9%) women in group (1) referred with negative cytology, there was one cancer (0.08%) and 22 high-grade squamous intraepithelial lesions on histopathology (HSIL (cervical intraepithelial neoplasia 2/3)). In group (2), there was no cancer or HSIL in 83 women with negative co-tests (negative for HPV oncogene and cytology). False negative cytology after negative reference cytology or co-test was low with 2% repeated cytology on initial colposcopy showing possible HSIL or worse. The authors conclude that women who have only postcoital bleeding and negative cytology have a low risk of cancer and could be tested for HPV before triage

on colposcopy. They found that with a negative joint test and a low probability of false-negative cytology, these women can avoid colposcopy unless clinical evidence of cervical cancer is suspected (8).

In this study, no significant difference in the age of first coitus was found between the examined groups (p = 0.768). The age of first coitus in subjects without condyloma was 19.0 (18.0-21.0), while in subjects with condyloma present 20.0 (17.0-22.5). A cross-sectional study conducted by Giuliano et al. showed that the age of 9 to 15 at the first sexual intercourse increases the risk of HPV infection (9), which is correlated with the results of this study.

In this study, a significant difference in the number of sexual partners was found between the examined groups (p = 0.018). The number of sexual partners in subjects without condyloma was 3.0 (2.0-4.0), while in subjects with condyloma present 4.0 (2.0-6.0). Other parameters did not differ significantly between the examined groups. Remschmidt et al. state that the number of sexual partners higher than 5 is independently associated with cervical HPV infection with a probability ratio of 3.5 (10). It can be concluded that the increase in the number of sexual partners is a reflection of the increased probability of HPV infection. The Al-Awadhi study shows that oncogenic HPV types are detected in about 35% of patients with genital warts and predominate in warts from one to six months (11).

It is common knowledge that genital warts may be epidemiological cofactors in the development of HSIL. However, in this study, no significant difference was observed in the presence of cervical dysplasia in subjects with the presence of condyloma compared to those without the presence of condyloma. Multivariate analysis by Wudtisan et al. showed that the history of genital warts was significantly associated with the development of HSIL in women younger than 30 years with an OR of 20.46 (95% CI, 2.27-183.72; P = 0.007) compared with women aged ≥ 30 years (4). Remschmidt et al. (10) report similarly.

Conclusion

Subjects with the presence of condyloma have statistically significantly more frequent postcoital bleeding, a larger number of partners and have started with sexual intercourse somewhat younger compared to subjects without the presence of condyloma.

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