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EVALUATION OF NON-VIRAL MICROBIOTA PRESENCE IN PATIENTS WITH DYSPLASIA AND CERVICAL CANCER

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ABSTRACT

Due to the increased incidence of cervical cancer in Romania, early detection of its causes and the taking of preventive measures are imperative.

In this sense, the aim of our study was to evaluate the infectious and non-infectious risk factors associated with the occurrence of dysplasia and cervical cancer.

We conducted a study that included 250 patients who presented themselves at the gynecological office of Policlinica 2 Constanta for specialist consultation (control or treatment) during 1 year. During their visits, Pap smear, tests for identify bacterial and fungic infections were collected together with responses to a questionnaire that evaluated the presence of socio-economical and other medical risks factor associated with dysplasia and cervical cancer..

The most important identified risk factors associated with the occurrence of cervical cancer are beginning sexual activity before the age of 16, pregnancy or abortion before the age of 18, use of empirical contraceptive methods, sexual relations with more than 3 partners during life.

Higher proportion of patients with displasya of cervical cancer presented infection with different types of non-viral microorganisms compared to women with normal results.

Keywords: cervical cancer, dysplasia,contraceptives, microbiota

Introduction

Cervical cancer is the fourth most frequently diagnosed cancer and the fourth leading cause of cancer death in women, with an estimated 604000 new cases and 342000 deaths worldwide in 2020 (1).

In Romania, Cervical cancer represents an important public health problem, despite its declining number of deaths and mortality rate, over the last two decades. Important differences are persisting between Romania and the EU and within the country, on the background of the failure in organizing a population-based national screening program (2). Approximately every two hours, a Romanian woman is diagnosed with cervical cancer as the country ranks first in the EU in terms of its mortality rate (3). In Romania, every year about 3,500 women are diagnosed with cervical cancer and 2,000 die from the disease (4)

The aim of the present study was to evaluate the presence of non-viral microbiota and non-infectious risk factors involved in the occurrence of cervical dysplasia and cervical cancer observed in women from South-East Romania, evaluated in an ambulatory gynaecological praxis.

Material and Method

In the study, 250 women were examined following the consultation within a gynaecological office. The sample was selected based on convenience, and biological samples were taken for analysis together with responses to a questionnaire that evaluates associated risk factors for cervical cancer. The patients were offered to complete a questionnaire that evaluated their age, marital status, age of initiating sexual activity, number of pregnancies, number of abortions, physiological status (menopausal status), contraceptive methods used (if any), total number of sexual partners, previous diagnosis of STDs, smoking status and history and environment.

According to the results from the biological testing, the women were divided into three groups: A - without significant changes, B - with cervical dysplasia in various stages, C - with cervical cancer.

The biological samples collected by the specialist doctor for performing Pap smear tests, bacteriological examinations, tests for the detection of Chlamydia T, Herpes s, etc., were transported to the Biomedical laboratory under safe conditions in isothermal bags with an accredited vehicle where they were processed using specific methods.

Results and discussions

According to the results of the Pap smear, patients were assigned to one of the following groups (Figure 1):

A: without significant clinical changes (81 cases);

B: different types of dysplasia (86 cases);

C: cervical carcinoma (CIS) confirmed histologically and colposcopically (83 cases).

We evaluated the presence of the risk factors. For the whole sample, 52.8% of the women had at least one risk factor. In the group of patients with cervical carcinoma all of the women had at least one risk factor associated with cervical cancer. The percentage dropped to 51.2% in the case of patients with dysplasia and was very low, 6.2% in the case of women without significant changes (Figure 2).

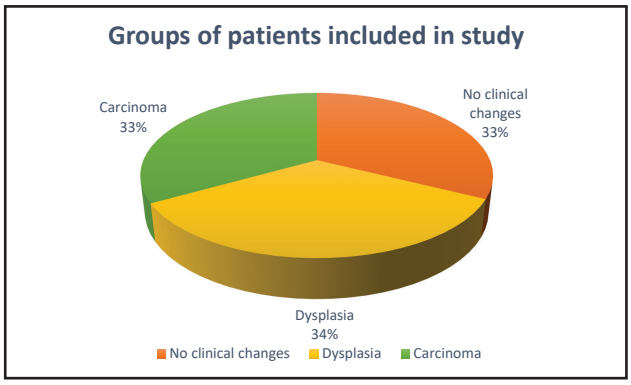


Figure 1 Distribution according to diagnosis

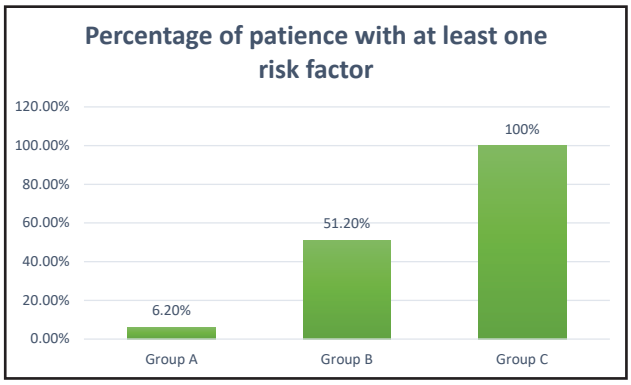


Figure 2 Percentage of patients with at least one risk factor

According to the type of risk factor, empirical use of contraceptives was identified in 42.1% of the women, followed by the previous diagnosis of STDs (38.7%). (Figure 3)

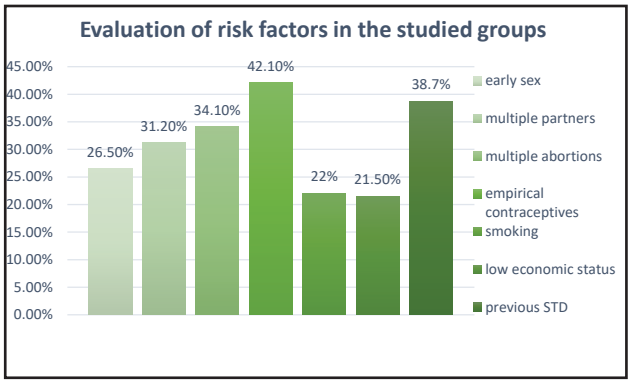


Figure 3 Prevalence of the risk factors

Vaginal secretions were investigated by direct gram-stained microscopic examinations and cultured on specific plates in order to identify bacteria or fungi. The associations between the presence of infections and the risk factors was also evaluated. In most of the cases, patients that

had at least one risk factor also presented higher percentages of infections. (Table 1)

Table 1 Frequency of infections in patients with or without risk factors

Infections	Risk factors (%)	No risk factors	p
Trichomonas vaginalis	35 %	27 %	0,18
Candida species	31 %	15 %	< 0,01
Morphological changes significant for HPV virus	5 %	0 %	0,01
Morphological changes significant for Herpes simplex virus	3 %	0 %	0,09
Shift in vaginal flora suggestive for bacterial vaginosis	14 %	9 %	0.28
Enterobacteriaceae	23 %	19 %	0.42
Gram-negative /gram-positive cocci	33 %	14 %	< 0,01

When we analysed the presence of microorganisms on each group, we observe that for trichomonas vaginalis and candida albicans the differences are significant ($p<0.001$), with higher percentages of infections detected in patients with dysplasia or cervical carcinoma. No statistically significant differences were observed in the case of Enterobacteriaceae or coccobacilli (Table 2).

Table 2 Frequency of infections by group

Infections	Group A	Group B	Group C	p
Trichomonas vaginalis	12%	62 %	51%	<0.001
Candida albicans	14%	47%	38%	<0.001
Gram-negative and gram-positive cocci	13%	29%	8%	0.001
Enterobacteriaceae	5%	5%	4%	0.91
Coccobacilli	9%	14%	12%	0.55

According to the results in this study, we observe the fact that, in patients with cervical dysplasia or cervical cancer, a higher percentage of women present dysbiosis, with different types of microorganisms. Statistically significant differences were observed in the case of trichomonas vaginalis, Candida albicans and different strains of cocci. Similar results were observed in other studies (5,6).

Currently we know that infection with specific strains of human papillomavirus is one of the main causes of cervical cancer (7), but few studies evaluated the role of the associated microbiota. Among these, some report the association between human papillomavirus and vaginal microbiota presence and diversity (8,9)

Conclusions

Non-viral microbiota is associated with a higher risk of cervical cancer, with higher percentages of women with abnormal pap smear tests presenting non-viral microbiota. Increasing the awareness of the risks that the presence of different vaginal infections have on the risk of developing cervical cancer might have a good impact on its incidence.

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