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Papillomavirus and cervical cancer: epidemiological study in a population of women in eastern Algeria

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ABSTRACT: Cervical cancer, predominantly caused by the human papillomavirus (HPV), is a significant public health issue in Algeria. While HPV is the primary pathogenic agent and sexually transmitted, other sexual and non-sexual factors also contribute as co-factors in the progression of HPV infection to cervical cancer. This study aims to identify the main risk factors associated with the development of cervical cancer in Algeria. The study included 54 women with cervical-vaginal smear abnormalities due to HPV infection, with an average age of 42.29 years (range: 25 to 65 years) and 7.40% being menopausal. Women married at an average age of 22.52 years, with 25.92% marrying before age 25 and 37.04% between 20 and 25 years. Parity ranged from 1 to 10 children, with an average of 4.96 births per woman. Among the women studied, 48.14% had an erosive cervix, 37.03% experienced cervix bleeding on contact, 11.11% had polypoid lesions, 7.4% were diabetic, and 7.4% had a history of recurrent genital infection. Cervical cancer is preventable through vigilant screening and early diagnosis. With an estimated incidence of 15.6 per 105,000 women annually, it ranks as the second most common cancer in Algerian women, leading to significant morbidity and mortality. Emphasizing the importance of timely detection, this study highlights the need for proactive measures to combat cervical cancer, reducing its human and financial burdens.

Keywords: Cervical cancer; Human papillomavirus; Precancerous lesions; Cervicovaginal smear; Diagnostic; Prevention.

1. INTRODUCTION

Cervical cancer is an infectious disease. It ranks second among female cancers worldwide, particularly in developing countries. In 2020, more than 604,000 new cases were diagnosed worldwide. In France, there were nearly 3,380 new cases and 1,450 deaths, according to the Léon Bernard Center for Cancer Control. Cervical cancer is ranked first in Africa with an intermediate incidence among Maghreb countries. The lowest incidence rates (less than 15/100,000) are observed in Europe (except for a few Eastern European countries), North America, and Japan [1].

Improving hygiene, lifestyle, and the organization of cervical cancer screening through cervical-vaginal smears (Pap smears) could decrease the incidence and mortality of this cancer [2]. Indeed, in Finland,

where organized screening covers 100% of the target population with conventional Pap smears every three to five years, the incidence is the lowest in the world. It ranges from 1.2 to 1.3 per 100,000 annually [3]. The major risk factor for cervical cancer is exposure to human papillomavirus (HPV). HPV is the commonest sexually transmitted viral infection worldwide [4]. This virus is transmitted through skin-to-skin and mucous membrane contact, most commonly through sexual intercourse [5]. However, other sexual and non-sexual factors act as cofactors in the progression of HPV infection to cervical cancer [6]. Infection with papillomavirus is extremely common, with an estimated 80% of women having been infected at least once in their lifetime. However, in approximately 10% of cases, the virus persists in the cervical mucosa. This can lead to changes in the epithelium, referred to as precancerous lesions, which have the potential to progress to cervical cancer. The primary sign of these lesions is genital bleeding [7].

In Algeria, cervical cancer ranks second among the most common cancers in the female population, with an estimated incidence of 15.6 per 105,000 women per year. It poses a significant public health problem and is one of the leading causes of morbidity and mortality [8].

The aim of researching the role of sexually transmitted infections in the development of cervical cancer from precancerous lesions and the involvement of certain factors is to screen these lesions in the at-risk population and prevent their progression to cancerous lesions [9,10].

Our study aims to determine the main risk factors involved in the occurrence and development of cervical cancer in Algeria, specifically within the female population in the eastern region of the country.

2. MATERIAL AND METHODS

2.1. Epidemiological data

Given the importance and the primordial role of the human Papillomavirus in the genesis of cervical cancer in the presence of cofactors and from precancerous lesions, a study was carried out over a period of two years 2020-2022 at the histology laboratory of the Constantine University Hospital.

At the time of conducting our research project, we are bound to comply with the decree on human ethics. The experimental protocol was approved by the Institutional Project Committee (PRFU, D01N01UN250120200012).

2.2. Cervicovaginal smear

The conventional screening cervical-vaginal smear (FCV) or Papanicolaou test is the best means of screening for precursor lesions of cervical cancer as well as cancerous lesions. It is a simple, painless and inexpensive screening test. It also makes it possible to detect certain specific cellular modifications of the causative agent, as is the case with sexually transmitted infections [3].

2.2.1. Questioning the patient

Before any sample, a midwife must imperatively fill out a form containing certain information essential for the interpretation of the slides and this form must be attached to the sample. The sheet includes surname, first name, address, age, gynecological history: age at menarche, frequency, age of first marriage, dates of last menstrual period, obstetrical history, number of procedures, and use or not a contraceptive method.

2.2.2. Direct debit conditions and sampling

The smear must be taken outside of menstruation, during the ovulatory period, away from any sexual intercourse, in the absence of bleeding and infection. After fixation of the speculum, the sample is taken at three

levels: sampling of the exocervix using an Ayer spatula, sampling of the endocervix or the endocervix junction using a swab and sampling Douglas's cul de sac using a tongue drop. Each sample is spread evenly on a clean slide without convolution or back-and-forth movement. The fixation must be rapid immediately after collection to preserve the morphology of the cells and their desiccation and to preserve their tinctorial affinities. Fixing is done in a conservation lacquer containing an acidified alcohol-based preservative 1% HCl-alcohol 95° for a minimum of 2 hours, or using a spray fixative. Papanicolaou staining is universally used in genital cytology. The reading of the smears is carried out using a light microscope by a doctor. The interpretation of the results is adopted by the classification of Bethesda (2001).

3. RESULTS

The sample for our study consisted of 54 women with cervical-vaginal smears showing lesions secondary to human papillomavirus (HPV) infection. These women had an average age of 42.29 years, ranging from 25 to 65 years. The obtained results highlight a proportional increase in the incidence of precancerous lesions of the uterus with age. Women aged between 40 and 49 years represent 37 % of the cases. The percentage is relatively low at 11% for age 25-29 and 7% for menopausal women (Figure 1).

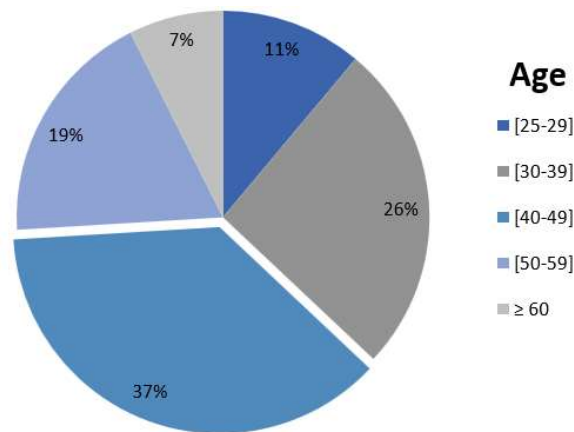


Figure 1. Distribution of smears with viral cervicovaginal lesions according to age.

The age of women at marriage varies from 18 to 30 years, with an average of 22.52 years. Fourteen women, accounting for 26%, married before age 20. In our series, a clear predominance is observed for women married between 20 and 25, with a percentage of 37% (Figure 2).

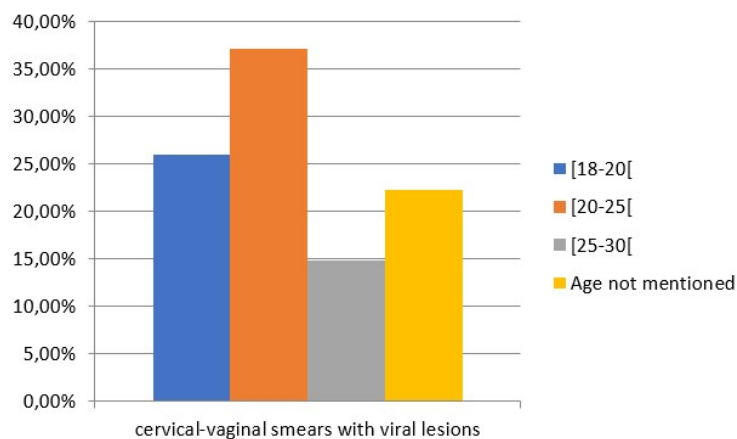


Figure 2. Distribution of cervical-vaginal smears with viral lesions according to age at first marriage.

The parity varies between 1 and 10 children, with an average of 4.96 births per woman. We observed an increase in the incidence of precancerous lesions of the cervix secondary to HPV infection based on the number of pregnancies. The group of grand multiparous women (parity of 6 or more) was the most representative in our study (38%). For multiparous women, i.e., those who have given birth at least 2 times but no more than 5 times, there were 32 cases, representing 61% (Figure 3).

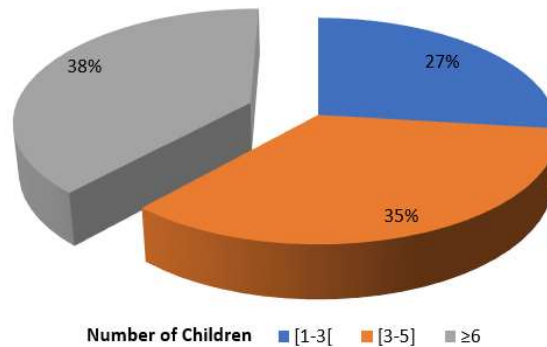


Figure 3. Distribution of cervical-vaginal smears with viral lesions according to the number of pregnancies.

4. DISCUSSION

The number of cases of cervical cancer recorded in Algeria annually according to the cancer register of the National Institute of Public Health (INSP) in 2019, about 1600 new cases, especially among those over 55 years old. In France, it is the 12th female cancer and the 10th leading cause of death from cancer in women [11]. In addition, the incidence of cervical cancer and mortality due to the disease remain high in Latin America and the Caribbean, and the number of cases of cervical cancer is expected to increase by 32%, with nearly 110,000 new cases in 2030 if no action is taken (30th Pan American Sanitary Conference, 2022).

Cervical cancer is by far the most common HPV-related disease. Almost all cases of cervical cancer can be attributed to HPV infection [12]. While most HPV infections are clear on their own and most precancerous lesions resolve spontaneously, there is a risk of progression from HPV infection to chronic disease or from precancerous lesions to invasive cervical cancer. all women [7]. Cervical cancer takes 15 to 20 years to develop in women with a normal immune system. It can take as little as 5 to 10 years in women with weakened immune systems, such as those with untreated HIV infection [13].

The results of our study on 54 patients with cervical lesions secondary to human papillomavirus infection are classified as precancerous lesions such as low-grade dysplasia (18.52%) and high-grade dysplasia (33.33%) caused by carcinogenic genotypes, and in condylomatous lesions (48.15%) caused by non-carcinogenic genotypes, but which does not exclude the presence of other carcinogenic genotypes. In our study, approximately 50% of the condylomatous lesions are associated with dysplastic lesions, and the other dysplasias are probably linked to human papillomavirus infection, according to the results of the cytological study correlated with the macroscopic examination of the cervix, and which have required biological confirmation which is not available at our level, therefore HPV is present in more than 90% of the cases in our study (Figure 4).

Through the results obtained in this research work, our collected data join those reported in the bibliography [14-16]. We find that viral intraepithelial squamous lesions appear with the highest rate between 40-49 years of age with a percentage of 37.04%. This result is far from the study [17] which reports that the average age of onset of cervical cancer is 51 years.

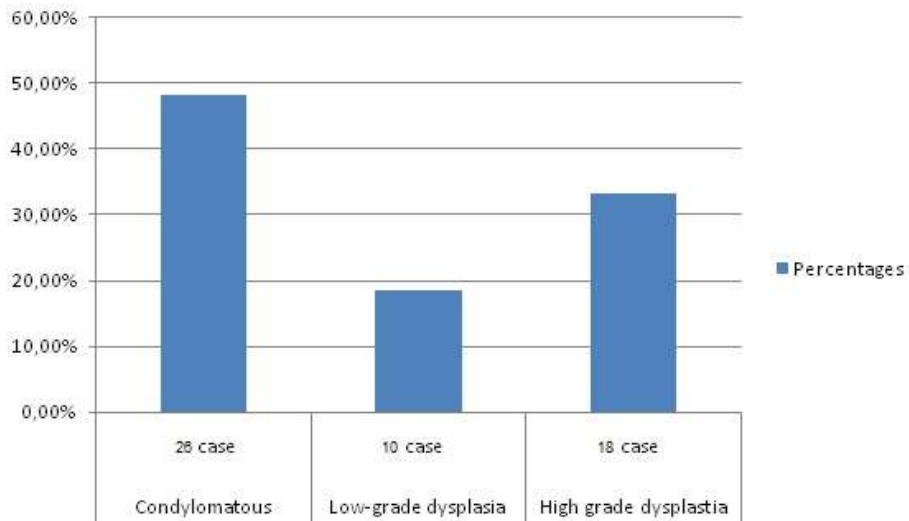


Figure 4. Distribution of cervicovaginal smears according to viral lesion.

On the other hand, our result is similar to that recorded in France, according to the epidemiological bulletin published in September 2019 by Public Health France, 40% of cases are diagnosed in women under 50, the median age being 53 and the highest incidence is seen in women aged 45-49. However, we observe a clear early marriage of our infected women (26%) for women aged between 18-20 against (15%) for those between 25-30. This precocity of marriage gives an approximate idea of the age of first sexual intercourse, the precocity of which constitutes a risk factor. The interval between the age of first marriage and the age of onset of viral lesions corresponds to a period of 10 to 15 years. A key factor is therefore the age of first sexual intercourse. The younger the woman is at her first sexual intercourse, the higher the risk of subsequent cervical cancer [18]. We also find that the prevalence of dysplastic and condylomatous lesions according to the number of pregnancies is found to be under a percentage of 27%, which represents women who have given birth at least once, and the percentage increases with the increase in the number of procedures 34.61% for women who gave birth [3-5] and 38.46% for grand multiparas who gave birth to more than 6 children. It can therefore be argued that gestation appears as a risk factor or cofactor favoring the occurrence of HPV infection, either generally by the physiological slowing down of the evolution of pregnancy on the general immune defense mechanisms, which favors the occurrence of viral or bacterial infections and others, Either locally linked to the biological upheaval suffered by the epithelium of the cervix during pregnancy [10,19]. Moreover, in our study, the risk factors that act as cofactors favoring the occurrence of dysplasia in the presence of the human papillomavirus are age, multiparity, earliness of first intercourse, immunosuppression, fragility of the cervix following chronic or recurrent genital infections caused by other germs responsible for sexually transmitted or other infections. These results are consistent with the work of [10,20,21]. We noted 37.04% of women with suggestive lesions with an erosive cervix (20 cases) and a bleeding cervix on contact (20 cases), this result is similar to that of [22]. Our series found a history of recurrent genital infection in 7.41% of patients. Women with recurrent genital infections are at greater risk of developing cervical cancer than those without [23]. In another case-control study, anti-*Chlamydia trachomatis* antibodies were found in 31% of cervical cancer cases compared to 11% in controls [24]. Among our 54 patients, 4 women (7.41%) were diabetic (Figure 5).

A woman with diabetes is about twice as likely to have uterine cancer as a woman without diabetes. Women with diabetes who are also obese or have high blood pressure are at even greater risk of developing uterine cancer [25]. In France INCa, reports related risk factors: prevalence of tobacco use, women aged 15 and

over 1%, condom use at last high-risk sex 46 %, HIV incidence per 1000 women aged 15+ 0.05%. Note that the condom, even if it limits contact with the virus, does not provide complete protection.

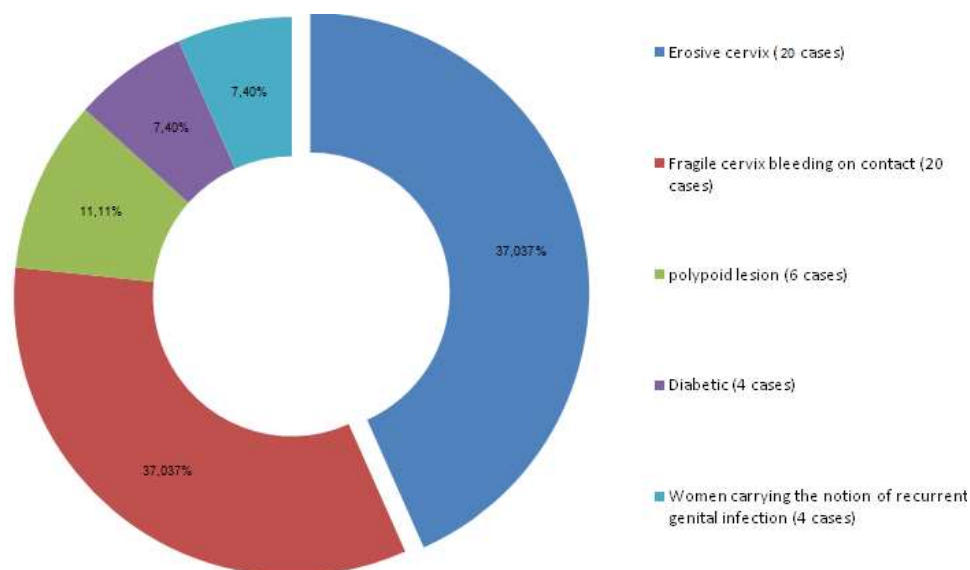


Figure 5. Distribution of cofactors according to 54 women cases.

5. CONCLUSION

The majority of our patients were diagnosed at advanced stages, hence the importance of emphasizing awareness and screening. The application of the cervicovaginal smear makes it possible to detect and treat precancerous lesions early and reduce invasive cancer rates by up to 80%. In our study, the sexual transmission of the "human papillomavirus" is the main etiology of cervical cancer. The young age of onset of sexual activity, and multiparity, are the main risk factors likely to potentiate the role of HPV. The risk factors that act as cofactors favoring the occurrence of dysplasia in the presence of the human papillomavirus are age, multiparity, earliness of first intercourse, diabetes, fragility of the cervix following chronic or repeated genital infections caused by other germs responsible for sexually transmitted or other infections.

Cancer of the uterus is a preventable cancer but we must remain vigilant. 90% of cancers could be prevented through screening. The later their diagnosis, the higher their human and financial costs will be. Prevention is based on two essential factors, namely the vaccine and early treatment.

Author's contribution: NS-A: Data collection from the registers of the histo-embryology laboratory at the CHU Constantine; Data processing; Writing the article. AK: Data collection from the registers of the histo-embryology laboratory at the CHU Constantine; Data processing; Translation of the article and formatting. Both authors read and approved the final version of the manuscript.

Ethics Statement: The study has been approved by the Institutional Project Committee (PRFU, D01N01UN250120200012).

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