Science World Publishing

Open Access Journal | Volume: 1.1

SCIENCE WORLD JOURNAL OF CANCER SCIENCE AND THERAPY

Crossref

Cervical Cancer: Definition, Prevention and Treatment

Mari Uyeda[1*]
Fabian Friedrich[2]
Antonio Cassio Assis Pellizzon[1]

[1]AC Camargo Cancer Center-Tamandaré St, 753 - Liberdade, São Paulo - Brazil, 01509-020. Department of Radiotherapy of the Hospital AC Camargo Cancer Center, São Paulo, Brazil

[2]Secretary of Health of the Municipality of Blumenau - Dois de Setembro St - Itoupava Norte, Blumenau - SC, 89052-001. Secretary of Health of the Municipality of Blumenau, Santa Catarina, Brazil

Article Information

Article Type: Review
Journal Type: Open Access
Volume: 1 **Issue:** 1
Manuscript ID: SWJCST-1-101
Publisher: Science World Publishing

Received Date: 03 January 2019
Accepted Date: 25 January 2019
Published Date: 27 January 2019

***Corresponding author:**

Mari Uyeda

AC Camargo Cancer Center-
Tamandaré St
753 - Liberdade
São Paulo - Brazil
01509-020
Department of Radiotherapy of the
Hospital AC Camargo Cancer Center
São Paulo
Brazil

Citation: Mari Uyeda: (2019) Cervical Cancer: Definition, Prevention and Treatment. Sci World J Cancer Sci Ther, 1(1);1-7

ABSTRACT

Cervical cancer is still considered a public health pathology in developing countries due to the lack of preventive examinations by the public health system and often due to other factors that place this neoplasm as the third cause of death in women in Brazil, especially in regions with lower financial and educational resources. Risk factors such as smoking, exposure to Human Papillomavirus (HPV), many sexual partners, onset of sexual activity before age 18, many pregnancies and poor hygiene still occur in the North, Northeast, and Midwest regions. Correct and early diagnosis are closely linked to success in treating and curing the disease. Treatment will depend on staging of the disease, and may be surgical or accompanied by chemotherapy and/or radiotherapy (Teletherapy and/or Brachytherapy). Primary prevention is also of paramount importance in the identification of pre-lesions that, if unidentified and properly treated, can progress to cancer and lead to death. Therefore, we can conclude that cervical cancer is still a disease that leads many women to death in developing countries and that it must be identified and treated immediately after its correct diagnosis and staging and, when the correct treatment happens, the chances of healing are greater than 80%.

KEYWORDS

Cervical cancer, Colo of uterus, Neoplasia, Pap Smear

BACKGROUND

Cervical Cancer (CC) is a malignant tumor where there is an exaggerated and disorganized multiplication of uterine cervix cells located at the bottom of the vagina. These changes are called precursor lesions, they are totally curable most of the time and, if left untreated, can, after many years, become cancer until they lead to death (Silva, 2017).

CC is considered a serious public health problem affecting women worldwide. In developing countries, it is responsible for 80% of mortality cases. It is the third most frequent tumor in the female population, behind breast and colorectal cancer, and in Brazil is the third cause of cancer death in women, excluding non-melanoma skin cancer. In 2012, estimates reached 528,000 new cases, of which about 80% occurred in less developed regions. The country has advanced in its ability to perform an early diagnosis, but 70% of the diagnosed cases were already with the invasive disease, that is, at its most advanced stage, but today there are at least 44% cases of precursor lesions in the cancer (Silva, 2017). In the North of Brazil, it is the most incident, and in the Midwest and Northeast, it occupies the second position. Regarding mortality, despite the fall observed in the country in recent years, it does not occur in all regions, such as in the interior of the North and Northeast (Corrêa et al., 2017).

The National Cancer Institute (INCA) estimates that for each year of the 2018/2019 biennium, 16,370 new cases of CC are diagnosed in Brazil, with an estimated risk of 15.43 cases per 100,000 women, occupying the third position (INCA, 2018).

Cervical precancers are diagnosed far more often than invasive CC. Most CC cases are diagnosed in women aged 35-44 years. It rarely

develops in women under the age of 20. Many older women do not realize that the risk of developing CC is still present with age. More than 15% of CC cases are diagnosed in women over 65 years of age (INCA, 2018).

There has been a decline in the number of deaths from this neoplasm since the 1930s, mainly related, but not exclusively, to the completion of the Pap smear examination. However, in developing countries CC remains a leading cause of death in women. Several factors contribute to this fact, such as the lack of programs for early detection, lack of adherence of women to these programs and the high rate of human papillomavirus (HPV) infection and cultural differences with respect to sexual activity.

Cervical

The cervical divides into the ectocervix and endocervix portions. The endocervix corresponds to the cervical canal and is covered by simple or cylindrical columnar epithelium, rarely ciliated and producing mucus. The endocervix begins at the internal bore continuously to the endometrium. In the standard colon the endocervical columnar epithelium terminates unexpectedly at the level of the external anatomic orifice. The ectocervix, the fundus of the sac and the vagina are lined by non-keratinized stratified squamous epithelium. In the encounter of different epithelium is called Escamo-Colunar Junction (JEC) or zone of transformation (Carvalho, 2009).

Cervical Cancer (CC)

It is a malignant tumor that develops from changes in the cervical, located at the bottom of the vagina. These changes are called precursor lesions, they are fully curable most of the time and, if left untreated, can, after many years, turn into cancer until they die. Precursor lesions or cancer when in early stages show no signs or symptoms, but as the disease progresses, vaginal bleeding, discharge and pain may not always appear in that order. (INCA, 2018).

Types of Tumor

There are two types of malignant tumors frequently associated with HPV infection: epidermoid carcinomas and adenocarcinomas. Squamous cells are those that cover the outer surface of the cervix.

In these cells can occur:

(i) Low-grade intraepithelial lesion (comprising cytopathologic effect by HPV and grade I cervical intraepithelial neoplasia);

(ii) High-grade intraepithelial lesion (including cervical intraepithelial neoplasms grades II and III);

(iii) high-grade intraepithelial lesion and cannot exclude micro-invasion;

(iv) Invasive epidermoid carcinoma.

Adenocarcinoma in situ and invasive adenocarcinoma (uterine and endometrial) can occur in glandular cells. In uterine adenocarcinoma, glandular cells are found in the cervical canal (Silva, 2017).

Endometrial cancers that start in cells lining the uterus belong to the group of carcinomas. Most endometrial carcinomas are cancer of the cells that form the endometrial glands (INCA, 2008; Koss & Gompel, 2006).

Histopathology

Squamous Cell Carcinomas (SCC) account for 70% of cases, adenocarcinomas 25%, and carcinomas Adenosquamous 3 to 5% (Seer, 2000). Adenosquamous carcinoma exhibits glandular and squamous differentiation and presents a worse prognosis than CC or adenocarcinomas (Diz & Medeiros, 2009).

One study found that the presence of adenocarcinomas is related to the greater chance of false negative results in the oncotic cytology examination and to a significantly shorter time between a negative Pap smear and the diagnosis of cancer when compared to the data for squamous cell carcinoma. A collaborative study group on the International Collaboration of Epidemiological Studies of Cervical Cancer analyzed data from 12 epidemiological studies and found that preventive screening reduced the risk of both histological subtypes but more importantly for squamous cell carcinoma (RR 0.46, 95% CI 0.42-0.50 versus RR 0.68, 95% CI 0.56 - 0.82) (Diz & Medeiros, 2009).

Neuroendocrine and small cell carcinomas can originate in the uterine cervix, but are rare. Primary rhabdomyosarcoma of cervical is a rare disease and occurs in young women and adolescents. Primary lymphoma of CC and sarcomas are other infrequent possibilities (Diz & Medeiros, 2009) (Table 1).

Staging of CC

Cancer staging (also called stages of cancer) is the description, usually in numbers from I to IV, of how much cancer has spread through the body (Uyeda et al., 2018).

In order to determine staging, a physical examination is performed with palpation of lymph nodes and vaginal and bimanual rectovaginal exams, and procedures such as colposcopy, hysteroscopy, biopsy and conization may be requested (Silva, 2017).

The stages I, II, III and IV are classified.

- Stage I: Regardless of its size, the cancer is located in the uterus;
- Stage II: Spreads beyond the cervix surrounding the vagina, but does not reach the bony wall of the pelvis;
- stage III: The cancer extends to the bony wall of the pelvis, involving the vagina and the lower third of it and Stage
- IV: The most advanced CC

The cancer has spread to neighboring organs or other parts of the body (INCA, 2014) (Table 2).

The CC can be spread by direct invasion of adjacent structures (Uterine body, vagina, parametries, peritoneal cavity, bladder and rectum) and by lymphatic (Pelvic, retroperitoneal and supraclavicular fossa) and hematogenic (Visceral metastases) dissemination (Diz & Medeiros, 2009).

CC staging, according to the 6th Edition of the AJCC (2002), can be performed by the TNM or FIGO classification, and takes into account the presence or absence of invasion, presence of macroscopic or microscopic disease, depth of stromal invasion, size of the lesion, invasion of adjacent structures, involvement of lymph nodes and presence or absence of metastases.

Table 1: Uterine Cervix Cancer-Histological Types

Squamous cell carcinoma	Clear Cell Adenocarcinoma
Large cell keratinizing squamous cell carcinoma	Serous adenocarcinoma
Large cell non-keratinizing squamous cell carcinoma	Mesenchymal adenocarcinoma
Verrucous carcinoma	Signet ring cell adenocarcinoma
Transitional cell carcinoma	Malignant adenoma
Lymphoepithelioma-like carcinoma	Adenocarcinoma viloglandular
Adenocarcinoma	Adenosquamous carcinoma
Endocervical (mucinous)	Cystic adenoid carcinoma
Endometrioid	Small Cell Carcinoma
Adenocarcinoma intestinal pattern	Undifferentiated carcinoma

Table 2: Staging of Cervical Cancer

TNM FIGO		
T - Primary Tumor		
Tx	-	Primary tumor cannot be detected
T0	-	No evidence of primary tumor
Tis	0	Carcinoma in situ
T1	I	Cervical carcinoma confined to the uterus
T1a	IA	Invasive carcinoma, diagnosed only by microscopy. All lesions visible macroscopically - even with superficial invasion - are T1b/IB Stage
T1a1	IA1	Stromal invasion of up to 3 mm in depth and 7 mm or less in horizontal extension
T1a2	IA2	Stromal invasion greater than 3 mm and up to 5 mm deep with a horizontal extension of 7 mm or less
T1b	IB	Clinically visible lesion, limited to the cervix, or microscopic lesion greater than T1a2 / IA2
T1b1	IB1	Clinically visible lesion with 4 cm or less in its largest dimension
	IB2	Clinically visible lesion larger than 4 cm in greatest dimension
T2	II	Tumor that invades beyond the uterus but does not reach the pelvic wall or the lower third of the vagina
T2a	IIA	No parametric invasion
T2b	IIB	With parametric invasion
T3	III	Tumor that extends to the pelvic wall, compromises the lower third of the vagina, or causes hydronephrosis or renal exclusion
T3a	IIIA	Tumor that compromises the lower third of the vagina without extension to the pelvic wall
T3b	IIIB	Tumor that extends to the pelvic wall, or causes hydronephrosis or renal exclusion
T4	IVA	Tumor that invades the bladder or rectal mucosa, or that extends beyond the true pelvis

Source: Diz & Medeiros, 2009

N: Regional lymph nodes*

NX: Regional lymph nodes cannot be evaluated

N0: Absence of regional lymph node metastasis

N1: Regional lymph node metastasis

M: Distant metastases

MX: The presence of distant metastasis cannot be evaluated

M0: Absence of distant metastasis

M1: Distant metastasis

*Regional lymph nodes include: paracervical, parametric, hypogastric (Ilial internal, obturator), common and external iliac, pre-sacral and sacral lateral.

Primary Prevention

Primary prevention of CC is related to decreased risk of HPV infection. The transmission of HPV infection occurs sexually, presumably through microscopic abrasions on the mucosa or skin of the anogenital region. Consequently, the use of condoms during sex with penetration partially protects from HPV infection, which can also occur through contact with the skin of the vulva, perineal region, perianal and scrotal pouch (INCA, 2017).

The HPV vaccine can prevent the virus from establishing persistent infections with significant organ damage. On the other hand, prevention tests (Especially the Pap smear) can detect the presence of so-called pre-cancerous lesions or CIN, which is extremely important, since it will allow early treatment, preventing the development of cancer in almost 100% of cases.

Secondary Prevention

Secondary prevention strategies for CC consist of early diagnosis of cervical lesions before they become invasive, from screening or screening techniques comprised of cancer colpo-cytology or Pap smears, colposcopy, cervicography, and, more recently, detection tests of HPV DNA in cytological smears or histopathological specimens. The colpocitological examination or Pap smear, among the methods of detection, is considered the most effective and efficient to be applied collectively in CC screening programs, being a technique widely diffused for more than 40 years, even without having been evaluated by means of experimental studies such as randomized clinical trials (Diz & Medeiros, 2009).

Treatment

HPV is transmitted by intimate contact unprotected with the individual infected by the virus, and can be transmitted by direct contact of the genitals during sexual practice, by anal intercourse that can result in viral infections and anal cancer, possibly by oral sex and during intercourse (Rosa et al., 2009). It presents a variable incubation period from 1 month to 2 years, and can be asymptomatic, and yet the infected person, in this condition, already transmits the virus. The INCA reports that several studies conducted worldwide prove that 80% of sexually active women will be infected by one or more types of HPV in their lives and in man the statistic is even greater. However, most of these infections are transient, and the body's immune system activity is effective in combating HPV. HPV is the main author of CC, but only virus infection is not sufficient for the disease to develop (Rosa et al., 2009).

CC treatment can be divided into treatment of early cases (FIGO IA, IB1, non-bulky IIA) and treatment of advanced disease (IIB - VAT).

Treatment of cases at an early stage (FIGO IA, IB1, non-bulky IIA)

Among the treatment options for early stage disease are:

1. Radical hysterectomy with pelvic/para-aortic lymphadenectomy with or without adjuvant chemotherapy and radiotherapy;
2. Radiotherapy and definitive chemotherapy;
3. Radical trachelectomy;
4. Conization.

Randomized trials suggest that overall survival is similar between radical hysterectomy (Including pelvic and para-aortic lymphadenectomy) with or without adjuvant radiotherapy and definitive chemotherapy for women with early-stage disease FIGO IA, IB1, non-bulky IIA (Diz & Medeiros, 2009).

Patients with very early stage disease (IA1 with no angio-lymphatic invasion) can be treated with simple hysterectomy, as the risk of regional lymph node involvement is very low (1%) (DIZ & MEDEIROS, 2009).

Patients with IA1 stages with angiolymphatic invasion, IA2 and IB1 are candidates for radical hysterectomy with pelvic/para-aortic lymphadenectomy.

Patients with stage IA disease or IB1 tumors smaller than 2 cm and who wish to preserve fertility are candidates for conservative surgery (Conization/trachelectomy), in which the body of the uterus is preserved.

Women who underwent hysterectomy and whose anatomopathological examination of the surgical specimen shows the presence of compromised or poor margins, the presence of lymph nodes involvement or microscopic invasion of the parametrium are risk factors for recurrence and these patients are candidates for adjuvant chemotherapy treatment and radiotherapy (Diz & Medeiros, 2009).

Although the optimal chemotherapy regimen is not established, the use of weekly cisplatin at a dose of 40 mg/m^2 (Cumulative minimum dose of 200 mg/m^2) is widely accepted and used in several centers around the world (Diz & Medeiros, 2009).

Treatment of stages IIB-VTA

For locally advanced disease there is no role for surgical treatment and the standard treatment is chemoradiotherapy (Teletherapy concomitant with chemotherapy followed by brachytherapy) (Diz & Medeiros, 2009).

Several randomized phase III trials have shown that the addition of chemotherapy as a radiosensitizer (Based on platinum derivatives) to radiotherapy increases progression-free survival rates and overall survival (Diz & Medeiros, 2009).

Treatment of recurrent or metastatic cases

The treatment of these cases is a challenge and requires multidisciplinary evaluation, involving teams of surgery, clinical oncology and radiotherapy (Diz & Medeiros, 2009).

Patients selected with local recurrence in the previously irradiated field are candidates for aggressive surgical resection (Pelvic exenteration), with long-term progression-free survival potential. In addition, non-irradiated patients may be candidates for rescue radiotherapy (Diz & Medeiros, 2009). Several cytotoxic agents have activity against metastatic CC. Cisplatin, which has a response rate of around 20%, is the most commonly used agent in clinical practice.

Other drugs with activity include: carboplatin, paclitaxel, topotecan, vinorelbine, gemcitabine and ifosfamide. Although symptom relief can be achieved with the use of these agents, the response duration is usually less than 3-4 months. The toxicity of therapy should be considered in clinical judgment, since patients with metastatic disease are often underperforming (Diz & Medeiros, 2009).

Objective response is more likely to be achieved in areas not previously irradiated and in patients not exposed prior to chemotherapy.

Schemes containing two drugs, such as cisplatin and paclitaxel or cisplatin and topotecan, present higher rates of objective response when compared to single drug regimens, but the combination of agents adds toxicity to treatment and should be considered only in carefully selected patients (Diz & Medeiros, 2009).

Symptoms

Early-stage cancer is often asymptomatic. When it manifests clinically, it does so with vaginal bleeding, dyspareunia and discharge, which may be aqueous, mucoid or purulent and foul. Pelvic and / or lumbar pain with irradiation to the posterior limb are usually symptoms of advanced disease (Silva, 2017).

More extreme cases may evolve with symptoms resulting from invasion / obstruction of adjacent structures, such as hematuria and ureterohydronephrosis secondary to invasion of the genitourinary tract or hematochezia and intestinal subocclusion by rectal invasion (Silva, 2017).

Risk factors

The various risk factors for the development of this tumor are known, such as HPV infection, smoking, early sexual initiation, multiplicity of partners, multiparity, use of oral contraceptives, low vitamin intake and coinfection with infectious agents such as HIV and Chlamydia trachomatis (Rodrigues et al., 2012). It is important to emphasize that there are no signs and symptoms that indicate lesions in the cervix, and when they arise they suggest the disease installed and the evolution to CC (Oliveira & Almeida, 2010).

HPV Infection

HPV is a member of the Papovaviral family, consisting of about 100 types of virus. Of these, approximately 50 affect the genital mucosa. The genomes of the virus are detected in the nucleus of the infected cells of the cervical and, often, HPV genomes integrated to the chromosomes can be evidenced in the majority of the lesions of high degree and, sometimes, in the lesions of low degree, this integration is the starting point in oncogenic cell transformation (Nakagawa et al., 2010).

Viruses can be classified as oncogenic risk being high risk or low risk, it is evident that chronic infection is persistent for some types of this virus, especially for types 16 and 18, and is the main risk factor for development of CC (Mendonça et al., 2011).

Silva & Silva (2012), report that it is estimated that approximately 80% of CC mortality is reduced when there is adequate screening of women between 25 and 64 years of age, as well as when there is early treatment of precursor lesions with high potential for malignancy or carcinoma *in situ*.

São Bento *et al*. (2010) refer to the importance of the HPV vaccine, the authors further point out that in the future, this vaccine will probably become an important strategy in the control of CC. The vaccine protects against the four major viral types: 6, 11, 16, and 18. The authors questioned the possibility of protection against other types by cross-protection. The vaccine can be administered in girls aged 9 to 25 years old and gives immunity of up to 98.9% against warts and 100% for CC, consisting of the administration of 3 doses intramuscularly.

From infection to the development of invasive neoplasia four stages are described:

1. Infection of the metaplastic epithelium of the transformation zone by oncogenic virus strain;
2. Persistence of infection;
3. Progression of a clone of infected epithelial cells to a precancerous lesion (Dysplasia; intraepithelial neoplasia);
4. Development of carcinoma with invasion of the basement membrane of the epithelium (Schiffman et al., 2007).

Smoking

Smoking is considered a risk factor for CC, according to Melo *et al*. In the study of the cervical epithelium of women smokers and non-smokers, there was a slight decrease in Langherans cells, since tobacco is responsible for the decrease in the number and functions of these cells, which are responsible for the defense of epithelial tissue. The decrease of these cells, facilitates the installation of viral lesions which are considered the first stage in the process of carcinogenesis.

In a study by Anjos *et al*. (2010), there is once again the association between risk factors for CC and smoking. In this study, the authors found that the results of positive Visual Acetic Acid (VTA) tests were more frequent the higher the level of Nicotine Dependence (QTF), and that women who smoked approximately 11 to 30 cigarettes per day showed a high rate of change in VAT exams.

Angels *et al*. (2013), when they evaluated the same nicotine dependence index in relation to the risk factors for CC, obtained similar results when they observed that "the higher the QTF the greater the nicotine dependence and, therefore, the greater the susceptibility to the development of cancerous lesions ".

Early Sexarch

According to Duarte *et al*. (2011), the sexarca before the age of 18 is classified as precocious because, at this age, the cervix is not yet fully formed and the hormonal levels are still destabilized. According to Silva & Silva (2012), the age group most affected by CC is 25 to 60 years. Young women are becoming a vulnerable population, precisely because of the onset of their precocious sexual life, which leaves them ever closer to diseases related to reproductive and sexual health. Melo *et al*. (2009) explain that the relationship between risk factors and CC in adolescents (Early sexual activity) refers to the area of transformation of the cervix which is located in the ectocervix (Outside the uterus) and is therefore more exposed to other risk agents as multiple partners and the non-use of condoms. Corroborating with the subject, Duarte *et al*. (2011) points out that the precocity of sexual activity is directly related to the increased risk of CC, since the cervical epithelial transformation zone is more proliferative during adolescence, making this population more vulnerable to cervical changes caused by sexually active agents communicable diseases.

A survey conducted by Anjos *et al*. (2010) found that most of the participants had the risk factor for CC related to the early onset of sexual activity, taking into account that the majority of the interviewees had their sex between 8 and 15 years, and the cytology tests were mostly women between 16 and 20 years of age.

In their study, Duarte *et al*. (2011) found a correlation between the risk factors and CC's establishment. In their findings, the majority of the members had sexual initiation in adolescence, which according to the authors counts another risk factor for CC, HPV contamination or other Sexually Transmitted Diseases (STD).

Multiplicity of Partners

The multiplicity of partners is a predisposing factor, since it facilitates the increase of sexually transmitted diseases (Melo *et al*., 2009). Duarte *et al*. (2011), states that "there is a higher incidence of cervical HPV lesions in women whose number of sexual partners, without condom use, is greater than two."

Two studies pointed out by Duarte *et al*. (2011) discuss the finding that women with HPV lesions, for the most part, had at least one intercourse without the use of condoms. The other study demonstrated an association between protection against HPV infection and a relationship considered stable.

A study by Melo et al. (2009) reported that most women had more than one sexual partner and, in the same study, women who had a single sexual partner showed a low frequency of lesions in relation to the others.

Multiparity

Women with more than four children (Multiparous) are the ones with the most cellular alterations in the exams. Data present in the study by Melo *et al*. (2009) note this statement, since most of the research participants who presented changes in the cytology were multiparous. We can relate multiparity and CC with biological mechanisms such as hormonal, nutritional and immunological.

A study by Ferreira & Galvão (2009) evaluated women from a textile industry at risk of cervical alterations, and found that more than 30% of women had this risk since this population had three or more children.

A research conducted by Rubini *et al*. (2012), in relation to women who already had CC, found that multiparous women were the ones that had the highest incidence of the disease. This finding justifies, confirms and affirms the relationship between the disease and its risk factors, recalling that the incidence of cervical cancer increases as early as sexual initiation and consequently lower the age of the first gestation, multiparity and multiple partners.

Use of Oral Contraceptives

Prolonged use of the contraceptive pill expands the transition zone which occasionally increases the chances of glandular tissue eversion and consequently leads to exposure to HPV aggression (São Bento *et al*., 2010). Melo *et al*. (2009) argue that the use of oral contraceptives induces sexual freedom, referring to the concern to avoid unwanted gestation.

Angels *et al*. (2010) found a relationship between the use of oral contraceptives, positive VTA tests and cervicographic examination. Regarding the cytology, the findings were different, since the positive results were evidenced in the women who did not use contraceptive and, of the women who used it, only one had a cytopathological alteration.

A recent analysis of 24 epidemiological studies found that among users of oral contraceptives, the risk of CC increases by 1.9 times according to the time of use when comparing women who used oral contraceptives for a period ≥ 5 years with those who were exposed to this treatment (RR 1.90, 95% CI 1.69-2.13). The risk declines after the interruption, and after 10 years again equals the rate of non-users. In the same study, the use of oral contraceptives for 10 years in the 20-30 age group increased the cumulative risk of cancer at age 50 from 7.3 to 8.3/1000 in developing countries and from 3.8 to 4.5/1000 in developed countries.

Low Vitamin Intake

Regarding the risk factors related to low intakes of vitamins and CC, only three authors reported on the subject, which had been approached superficially. For Oliveira (2010), Duarte *et al*. (2011) and Diógenes *et al*. (2012), the risk factors related to low intakes of vitamins and CC are: poor diet in some micronutrient antioxidants mainly vitamin C, beta carotene and folate.

Co-Infection by Infectious Agents: HIV and Chlamydia Trachomatis

Women who have some Sexually Transmitted Disease (STD) present five times more CCU precursor lesions than women who do not have any STDs (OLIVEIRA, 2010). Ferreira & Galvão (2009) establish that there are some risk factors considered decisive for CC, among them the history or partner with sexually transmitted infection. The authors also point out that the exposure of the cervix to some agent that causes a sexually transmitted disease, associated with conditions such as inflammatory processes or ectopia, facilitates the first contact with HPV, thus incurring a possible evolution for neoplasia of the genital tract bottom.

Angels *et al*. (2010) demonstrated in their study that among the interviewees who reported some type of STD, half presented positive VTA and the other half, negative. The most frequently reported STD was gonorrhea, followed by trichomoniasis and HPV/condyloma. It is noteworthy that all the interviewees had cytology results within the parameters of normality.

Other Found Risk Factors

São Bento *et al*. (2010), add a risk factor that was not evidenced. They defend the idea that the lack of hygiene of the penis is related to the occurrence of CC and also point out that in groups where there is the custom of performing the circumcision, the CC is lower among the female population. The authors state that "A woman invaded by her dirty partner, often because she cannot defend herself (Violence), cannot keep her lap clean."

Melo *et al*. (2009) in her research with 65 women with alterations in oncology cytology showed that a new age group is being reached earlier than previously thought. Approximately 21.5% of the women with cytological alterations are in age groups lower than those commonly found, since the incidence of the disease is around 40 to 60 years of age, and only a small percentage occurs before the age of 30 years. From 80% to 90% of cancers are determined by environmental factors, and age is an important determinant of cancer risk, and can occur at any other age, but it is much more common in people of advanced age. CC is directly related to unfavorable socioeconomic conditions. The CC is precociously detectable, it is curable and treatable (INCA, 2008).

Teenage girls under the age of 15 have a low risk of developing cervical cancer, the risk increases from 20 to 30 years. Women over the age of 40 are still at risk and should be continuously taking the Pap test. HIV infection is a risk factor because a woman with HIV-positive has fewer conditions to quell early cancers because she has a suppressed immune system, as well as women who are on systemic corticosteroids, therapies for other tumors and transplants; female smokers have two more opportunities to develop a CC than non-smokers, women with low socioeconomic status have greater risks, as they probably do not take preventive exams regularly (Silva, 2017).

For Brazil (2013), CC does not have a definite cause and can present many correlated factors that increase the chances of making the cervical abnormal, being able to cite the number of sexual partners, the greater the number of partners the greater the probability of being a carrier HPV virus which substantially increases the chance of developing a higher-grade lesion for invasive cancer.

CONCLUSION

With this small review, we can conclude that cervical cancer is still a very important disease in developing countries, occupying the third position in death of women in adulthood. Factors such as smoking, early sexarch, many partners and multiparity become risk factors if added to inadequate and late prevention. Correct diagnosis and staging of the disease are of primary importance in order to have the effective treatment and in this case the cure becomes more than 80%. Primary prevention of the disease is of importance in controlling the spread and evolution of precancerous lesions to cancer.

Acknowledgements

Antonio Cassio Assis Pellizzon and Fabian Friedrich for correction of the manuscript.

Availability of Data and Materials

The data that support the findings of this study are available from https://www.ncbi.nlm.nih.gov/pubmed.

Authors' Contributions

MU, MD was responsible for the research and writing of this manuscript. FF, MD, PhD was responsible for the research and revision of this manuscript. ACAP, MD; PhD was responsible for the revision of this manuscript.

Ethics Approval and Consent to Participate

Not Applicable

Consent for Publication

I, Mari Uyeda give my consente for publishing the literature review entitled: Cervical Cancer: Definition, Prevention, and Treatment.

I, Fabian Friedrich give my consente for publishing the literature review entitled: Cervical Cancer: Definition, Prevention, and Treatment.

I, Antonio Cassio Assis Pellizzon, MD; PhD give my consente for publishing the literature review entitled: Cervical Cancer: Definition, Prevention, and Treatment.

Funding

There was no funding provided for this study.

Competing Interests

The authors declare that they have no competing interests.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

BIBLIOGRAPHY

1. Silva AA. Cervical Cancer: The importance of cytology examination in its prevention. Graduation in Nursing-Metropolitan Union of Education and Culture, Lauro de Freitas. 2017.
2. Corrêa CSL, Lima AS, Leite ICG, Pereira LC, Nogueira MC, et al. Cervical cancer screening in Minas Gerais: Evaluation based on information from the Cervical Cancer Information System (SISCOLO). Cad Saúde Colet. 2017;25(3):315-323.
3. National Cancer Institute. Cancer of the Cervical Cancer. 2018.
4. Carvalho G. Cytology of the female genital tract, 5th Edi., Revinter, Brazil. 2009.
5. National Institute of Cancer, INCA. Nursing actions for cancer control: A proposal of teaching-service integration. 3rd Edi, Rio de Janeiro: INCA. 2008.
6. Koss LG, Gompel C. Introduction to gynecological cytopathology with histological and clinical correlations, Roca, São Paulo-SP. 2006.
7. http://seer.camcer.gov/
8. Diz MDPE, Medeiros RB. Cervical cancer-risk factors, prevention, diagnosis and treatment. Rev Med (São Paulo). 2009;88(1):7-15.
9. Uyeda M, Friedrich F, Pellizzon ACA. High Dose Rate (HDR) Brachytherapy in the Gynecological Cancer: a literature review. Appl Cancer Res. 2018;38:19.
10. National Cancer Institute. José Alencar Gomes da Silva. Monitoring of actions to control cervical and breast cancers. Informational Early Detection. 2014;5(1):1-8.
11. Rosa et al. Human papillomavirus and cervical neoplasia Cad. Saúde Pública. 2009;25(5).
12. Rodrigues BM et.al. Health Education for the Prevention of Cervical-Uterine Cancer. Brazilian Journal of Medical Education. 2012;36(1, Suppl 1):149-154.
13. Oliveira SL, Almeida ACH. The Perception of Women in the Face of the Pap Smear: from Observation to Understanding. Cogitare Nursing. 2009:14(3):518-526.
14. Nakagawa JTT, Schirmer J, Barbieri M. HPV virus and cervical cancer. Revista Brasileira de Enfermagem, Brasília. 2010;63(2):307-311.
15. Mendonça FAC et.al. Prevention of Cervical Cancer: Adherence of Primary Care Nurses and Users. Journal of the Nursing Network of the Northeast, Fortaleza. 2011;12(2):261-270.
16. Schiffman M, Castle PE, Jeronimo J, Rodriguez AC, Wacholder S. Human papillomavirus and cervical cancer. Lancet. 2007;370(9590):890-907.
17. Melo SCCS, Prates L, Carvalho, MDB, Marcon SS, Pelloso, SM. Cytopathologic Alterations and Risk Factors for the Occurrence of Cervical Cancer. Revista Gaúcha de Enfermagem, Porto Alegre (RS). 2009;30(4):602-608.
18. Ferreira, MLSM, Galvão MTG. Risk Assessment of Uterine Cervical Cancer in Textile Industry Workers. Science Care and Health. 2009;8(1):86-92.

19. Anjos SJSB, et al. Risk Factors for Cervical Cancer of the Uterus According to VAT, Cytology and Cervicography Results. Revista Escola de Enfermagem USP São Paulo. 2010;44(4)912-920.
20. Anjos SJSB, et al. Risk factors for cervical cancer in female inmates. Revista Brasileira de Enfermagem, Brasília, Brazil. 2013;66(4):508-513.
21. Duarte SJH, Matos KF, Oliveira PJM, Matsumoto AH, Morita LHM. Risk Factors for Cervical Cancer in Women Assisted by a Family Health Team in Cuiabá, MT, Brazil. Ciencia Y Enfermeria. 2011;17(1).
22. Silva MRB, Silva GP. Knowledge, Attitudes and Practice in the Prevention of Uterine Cancer of a Unit in the West Zone of Rio de Janeiro. Revista de Pesquisa: Cuidado é Fundamental online. 2012;4(3):2483-2492.
23. Rubini AMS, Santos JLG, Erdmann AL, Rosa LM. Speeches of Women with Cervical Cancer in Brachytherapy Treatment: Nursing Care Subsidies. Nursing Journal of UFSM. 2012;2(3):601-609.
24. São Bento PAS, Telles AC, Suzarte CTS, Moraes LEO. Cervical Cancer of the Uterus As Phantom Resistant to Primary Prevention of Early Detection. Research Journal: Care is Fundamental Online.2010;2(2):776-786.
25. Oliveira TC. Performance Evaluation of the Cervical Cancer Control Program: a model for local application in the city of Rio de Janeiro. 78 f. Thesis (Master in Public Health) Rio de Janeiro: sn, 2010.
26. Diógenes MAR, Cesarino MCF, Jorge RJB, Queiroz INB, Mendes RS. Risk Factors for Cervical Cancer and Adhesion to the Papanicolau Exam Among Nursing Workers. Journal of Nursing Network of the Northeast. 2012;13(1):200-210.
27. Brazil. Ministry of Health. Secretariat of Health Care. Department of Basic Attention. Tracking. Brasília: Ministry of Health; 2013 (Series A. Standards and Technical Manuals, Primary Care Notebooks, 29).