

# Cancer of cervix: epidemiology, risk factors, stage and management

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ABSTRACT

In female cervical cancer is one of the top causes of death from cancer worldwide and its behavior epidemiologically likes a venereal disease of low infectiousness. Major risk of cervical cancer is early age at first intercourse and several sexual partners have been shown to exert strong effects. The wide differences in the prevalence amid different countries also influenced by the introduction of screening. While the common picture remains one of decreasing prevalence and death, there are signs of an increasing cervical cancer risk possibly due to changes in sexual behavior. Other important factors are smoking and human papilloma virus is currently important issues in a concept of multi factorial, stepwise carcinogenesis at the cervix uteri.

**Keywords:** cervix cancer, epidemiology, risk factors, stage and screening

## INTRODUCTION

Cancer of Cervix is the second most important malignant tumor worldwide which seriously threatens female's health. Constant infection of elevated risk Human Papilloma Virus (HPV) has been clarified to be the essential reason of cervical cancer in female [1]. The clear etiology accelerated the concern and implementation of comprehensive preclusion and control system of cancer of cervix in female. In May 2018, the World Health Organization issued a call for the elimination of cervix cancer worldwide, and more than 70 countries and international academic societies acted positively instantly [2]. At this landmark time point, we reviewed the update evolution of cancer of cervix prevention and control in epidemiology, risk factors and screening, in order to pave the way of cancer of cervix exclusion worldwide [3].

## Epidemiology

In women Cancer of Cervix is one of the most important causes of cancer death. In last 30 years, cervical cancer has increased ranged from 10 % to 40 % in young women. WHO and International Agency for Research on Cancer (IARC) estimates, the year 2008 saw 529,000 fresh cases record of cervix cancer worldwide. Number of fresh cases of cancer cervix reached to 452,000 and second most malignant cancer in the female patients. On the other hand, the number of new patients of cervical cancer was 77,000 in developed nation and ranked tenth among malignancies in female [4, 5].

## Risk factors of cervical cancer

A numerous risk factors for cervix cancer are associated to exposure to the HPV. Invasive cancer development process could delay up to 20 years from the precursor lesion caused by sexually transmitted HPV. However, there are also other several risk factors (like as reproductive factors and sexual factors, behavioral factors, etc.) for cervix cancers which consist of sexual intercourse at a young age (<16 years old), multiple sex partners, smoking, high parity and low socio-economic status of patients [6, 7].

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## Stage of cervical cancer

### Sexually Transmitted Infections (STI) HPV:

Infection is the most important reason of pre cancerous and cancerous cervix lesions with a high-risk or oncogenic HPV variety. Major case of cervical cancer happen as a end result of infection with HPV 16 and 18. HPV16, are establish to be extremely prevalent in human populations. The sexually transmitted infection is generally transmitted by sexual contact, causing squamous intraepithelial lesions. The majority of lesions vanish after 6 months to 12 months due to immunological intervention. But, a minute percentage of squamous intraepithelial lesions stay and can cause cancer of cervix. The outcome of a meta-analysis study showed that the highest incidence of HPV occurs at the age of 25 years, which could be associated to changes in sexual behavior.

### Human Immunodeficiency Virus (HIV)

The risk of developing cervical infection from high risk HPV types is high in women with HIV infection. The outcome of the study on the relationship among HIV and cervical cancer suggested a higher rate of persistent HPV infection with several oncogene viruses, additional abnormal Papanicolaou (Pap) smears, and higher prevalence of CIN and invasive cervix cancer among people with HIV. Those women who infected with HIV are at increased risk of HPV infection at an early age (13 years-18 years) and are at high risk of cervix cancer. Compared with non-infected women, HIV positive patients with cervical cancer are diagnosed at an earlier age (15 years-49 years old).

## Reproductive and sexual factors

### Sexual partners:

Cervical cancer has also connected with most important factor like sexual behavior. Outcome of one study shown that increased risk of cervical cancer is observed in those people with have multiple sex partners. – Furthermore, numerous studies have also recommended that women with several sexual partners are at increased risk for HPV acquisition and cervical cancer. In the meta analysis, a considerable high risk of cervical cancer and other diseases was observed in individuals with several sexual partners compared to individuals with single number of partners, both in non-malignant cervical disease and in cervical malignancy. Also, early age at first intercourse is a risk cause for cervical cancer.

### Oral Contraceptive (OC) pills

The other risk factor of cervical cancer is oral contraceptive pills. In an international collaborative epidemiological study of cervical cancer, the relative risk in existing users increased with an increase in the duration of Oral contraceptive pills use. It has been reported that the use of Oral contraceptive pills for 5 years or more can double the risk of cancer of cervix. a multi-center case control study shown, among women who tested positive for HPV DNA, the risk of cervical cancer increased by 3 times if they have used Oral contraceptive pills for 5 years or more . This study concluded that use of Oral contraceptive pills is an autonomous risk cause in causing cervical cancer (Table 1).

**Tab. 1.** International Federation of Gynecology and Obstetrics (FIGO) staging

Stages	Definition
IA	Invasive cervical carcinoma diagnosed by microscopy only, maximum depth of invasion <5 mm.
IA1	Measured stromal invasion <3 mm in depth.
IA2	Measured stromal invasion ≥ 3 mm and <5 mm in depth.
IB	Lesion is clinically visible, confined to the cervix or microscopic lesion greater than IA2.
IB1	Invasive carcinoma ≥5 mm depth of stromal invasion, and <2 cm in greatest dimension.
IB2	Invasive carcinoma ≥ 2 cm and <4 cm in greatest dimension.
IB3	Invasive carcinoma ≥ 4 cm in greatest dimension.
II	Cervical carcinoma involves beyond the uterus but not reach to pelvic wall or to lower third part of vagina.

IIA	Tumor without parametrial invasion or involvement of the lower one-third part of the vagina.
IIA1	Lesion visible clinically <4 cm in greatest dimension with involvement of less than the upper 2/3 of the vagina.
IIA2	Clinically visible lesion >4 cm in greatest dimension with involvement of less than the upper 2/3 of the vagina.
IIB	Tumor with parametrial invasion but not up to the pelvic wall.
III	Tumor extends to pelvic wall and/or involves lower third of vagina, and/or hydro nephrosis or nonfunctioning kidney, and/or involves pelvic and/or para aortic lymph nodes are present
IIIA	Tumor involves lower third of vagina, not extension to pelvic wall.
IIIB	Tumor extends to pelvic wall and/or hydro nephrosis or nonfunctioning kidney symptoms present.
IIIC	Tumor involves pelvic and/or para aortic lymph nodes, irrespective of tumor size and extent.
IV	Tumor invades mucosa of bladder or rectum (biopsy proven), and/or extends beyond true pelvis.
IVA	Tumor has spread to adjacent pelvic organs.
IVB	Tumor has spread to distant organs.

## MANAGEMENT

The main strategies or aim to prevent cervical cancer remain key in reducing the burden of the disease in the female. The focus of this review is, therefore, on treatment choice for cervical carcinoma in female.

In starting or in the early stage of cancer is more or less without any symptoms and may be diagnosed during schedule screening or pelvic examination. Excessive or abnormal vaginal bleeding, in particular following intercourse. In some female vaginal discharge present. That vaginal discharge may be watery, mucoid or mucopurulent with odors. On the other hand it is rarely seen in isolation of other symptoms. In advanced of disease, oedema in lower limb, flank pain, as well as pelvic or pain in lower back may be experienced by the patients. Several other symptoms like, bowel and/or bladder related problems like changes in pressure, bowel related or the passage of urine and/or faces through the vagina indicate invasion of the bladder and rectum respectively.

If any symptoms of cervix cancer and involves visualization of the cervix and vaginal mucosa only pelvic examination done but any abnormality shows we goes for biopsy. In case of micro invasive or in the endocervical canal cervix might appear normal. Large tumors on the other hand may show to completely

replace the cervix and metastatic lesions may be identified through enlarged palpable lymph nodes.

Colposcopy is perform for confirm diagnosis if a patient presents with a Pap smear result suggestive of a High Grade Precancerous Lesion (HSIL), or recurrent low grade cytology (LSIL), and for further analysis any questionable lesions biopsied. If a precancerous lesion is confirmed by colposcopy findings and/or biopsy, a therapeutic procedure called Large Loop Excision of the Transformation Zone (LLETZ) can be performed to excise the precancerous cells and prevent cancer. The stage of cervical cancer is an important prognostic marker and is determined clinically, based on size of tumor and degree of pelvic extension and imaging. Importantly, the stage of disease is assigned at the point of diagnosis and accurate staging is critical in treatment planning, counseling patients regarding prognosis, and evaluation of eligibility for research studies [8, 9].

## TREATMENT

- Surgery
- Chemotherapy
- Radiotherapy
- Immunotherapy
- Genetic approach

## CONCLUSION

The disease burden of cervical cancer has decreased significantly in developed countries and regions in last decades, however it is still serious in less developed countries and regions, and effective preventive measures in these areas still face serious challenges. At present, there are various available prevention and control measures that are cost-effective and scientific evidence-based to meet the needs of areas with different

economic levels. It is gratifying to note that the globe has achieved a strategic consensus on the elimination of cervical cancer and also has developed and released the global strategy to accelerate the elimination of cervical cancer. Although the global elimination of cervical cancer has a long way to go, it is believed that through large-scale continuous promotion and widely use of existing effective prevention and control measures, cervical cancer will become the first cancer eliminated by human beings.

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