Cervical cancer

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Female Genital Cancers

☐ Ovarian Ca. with. Bad prognosis is the 7thCancer in women

☐ Cervical Ca. with Milled prognosis is us the 2nd Cancer in women

☐ Endometrial Ca. with Good prognosis is the 8th. Cancer in women

Type of cervical Cancer

☐ Squamous Cell Ca. = 76 % - 90%

☐ Adeno Ca. = 10% - 13%

Progress of cancer

☐ From Normal Epithelium to Dysplasia to insitu Carcinoma to invasive Carcinoma takes long 8(9%) 15 (35%) -20 years

So we have enough time for screening

Incidence and mortality

Globally, cervical cancer accounted for an estimated 528,000 new cancer cases worldwide and for 266,000 deaths in 2012 .

Global incidence and mortality rates depend upon the presence of screening programs for cervical precancer and cancer and of human papillomavirus (HPV) vaccination, which are most likely to be available in developed countries. Due to these interventions, there has been a 75 percent decrease in the incidence and mortality of cervical cancer over the past 50 years in developed countries .

Eighty-four percent of cervical cancer cases were from less developed regions. In women in developing countries, cervical cancer was the second most common type of cancer (15.7 per 100,000 women) and the third most common cause of cancer mortality (8.3 per 100,000). On the continent of Africa and in Central America, cervical cancer is the leading cause of cancer-related mortality among women.

In developed countries in 2012, cervical cancer was the eleventh most common type of cancer in women (9.9 per 100,000 women) and the ninth most common cause of cancer mortality (3.3 per 100,000) . In the United States, almost 13,000 new cases of invasive cervical cancer and approximately 4100 cancer-related deaths occur each year .Cervical cancer is the third most common cancer diagnosis and cause of death among gynecologic cancers in the United States, with lower incidence and mortality rates than uterine corpus or ovarian cancer.
Cervical cancer estimates are higher for certain racial and ethnic groups: white (incidence: 7.1/100,000 and mortality: 2.0/100,000), non-Hispanic black (10.2/100,000 and 4.2/100,000), Hispanic/Latino (10.5/100,000 and 2.8/100,000), Asian/Pacific Islander (6.4/100,000 and 1.8/100,000), and American Indian/Alaska Native (9.7/100,000 and 3.4/100,000) .
In the era of HPV vaccination, most experts expect a decrease in the incidence of cervical cancer in women who receive the vaccine.
By some estimates, if vaccine rates of 70 percent worldwide are achieved, we would expect to see a decrease of 344,520 new cases of cervical cancer
annually and avoid 178,182 cervical cancer-related deaths .However, due to the latency period of 10 to 15 years between HPV exposure and cervical cancer development, there are not likely to be significant decreases in cervical dysplasia or cancer for many years after the implementation of vaccination programs.
Surprisingly, in countries such as Australia that have achieved vaccination rates >70 percent, there has already been a 38 percent reduction in high grade dysplasia .Even in countries with lower vaccination rates, such as the United States, for example, there has been a
decrease in the incidence of high grade cervical dysplasia. As an example, in Connecticut between 2008 and 2011, the vaccination rate increased from 45 to 61 percent. During that same time period, there was a decrease in high grade cervical dysplasia of 18 percent .As high grade dysplasia is a necessary precursor for squamous, adenocarcinoma, and adenosquamous

carcinomas of the cervix, this sharp decrease in high grade cervical dysplasia should translate
into decreased incidence of cervical cancer in the next decade.

Age

Worldwide in 2012, the cumulative risks of developing cervical cancer and of cervical cancer mortality by age 74 years were: developed countries (0.9 percent incidence/0.3 percent mortality) and developing countries (1.6 percent/0.9 percent) .
The lifetime risk of developing cervical cancer for United States women, based upon national data from 2000 to 2004, was 0.76 percent .The mean age at diagnosis of cervical cancer in the United States from 2000 to 2004 was 48 years. Only 5.7 percent of cases were diagnosed in women age 85 years or older. From 2000 to 2004, the United States age-adjusted incidence of cervical cancer in girls under age 20 was 0.1 per 100,000, rising to 1.5 per 100,000 in women age 20 to 24 years, and then ranging from 11.0 to 15.8 per 100,000 for women age 30 to over 85 years

Race and ethnic and religion

The incidence in Negros is two times more than white. The Hispanic and American
Indian have moderate situation and white people have the lowest rate.
Incidence in Japanese and Jewish the rates are low.
According to religion in Christian there are the highest rates after that in Islamic
person and at lost in Jewish people.

Cervical cancer is seen in low socioeconomic people more than high socio.

Risk factors

The two major histological types of cervical cancer, adeno carcinoma and squamous cell carcinoma, and the preinvasive disease that corresponds with these histologies share many of the same risk factor. Most of these are associated with an increased risk of acquiring or having appropriate compromised immune response to infection with HPV, the etiologic agent of most cervical cancers. These include:

●Early onset of sexual activity –

Compared with age at first intercourse of 21 years or older, the

risk is approximately 1.5-fold for 18 to 20 years and twofold for younger than 18 years

●Multiple sexual partners – Compared with one partner, the risk is approximately twofold with
two partners and threefold with six or more partners

●A high-risk sexual partner (eg, a partner with multiple sexual partners or known HPV infection)

●History of sexually transmitted infections (eg, Chlamydia trachomatis, genital herpes)

●History of vulvar or vaginal squamous intraepithelial neoplasia or cancer (HPV infection is also the etiology of most cases of these conditions)

●Immune suppress ioncioeconomic (eg, human immunodeficiency virus infection)

Cervical cancer is less common in sexual partners of circumcised males . Early age at first birth (younger than 20 years old) and increasing parity (3 or more full term births) are also associated with an increased risk of cervical cancer; these are also likely due to
exposure to HPV through sexual intercourse .

socioeconomic status

Low socioeconomic status is associated with an increased risk of cervical cancer. From 1988 to
1992 in the United States, cervical cancer incidence was higher in women who lived in communities with higher poverty levels (≥20 percent or more of the population below the
poverty level: 19.2 cases per 100,000 women versus <10 percent below poverty level: 8.8 per 100,000). Women in high compared with low poverty counties had a 71 percent higher rate of cervical cancer mortality.
In the United States, cervical cancer incidence and mortality is higher in nonwhite than in white women.

Oral contraceptive

It has been reported that the usage of oral contraceptive pills is associated with an increased risk of cervical cancer.

A collaborative analysis of data from 24 epidemiological studies found that among current users of oral contraceptives, the risk of invasive cervical cancer increased with increasing

Duration of use

More than 5 years use versus never-use has relative risk [RR] 1.90, 95% CI 1.69-2.13).

The risk declined after use ceased, and by 10 or more years, had returned to that of never users. In the same study, use of oral contraceptives for 10 years from age 20 to 30 years was estimated to increase the cumulative incidence of invasive cervical cancer by age 50 from 7.3 to 8.3 per 1000 in developing countries and from 3.8 to 4.5 per 1000 in developed countries.

While some studies suggest that adenocarcinoma appears to have a stronger association with oral contraceptives than does squamous cell cancer, others found a similar risk increase with increasing duration of oral contraceptives for both adeno- and squamous cell carcinomas .

In contrast to squamous cell cancer of the cervix, cigarette smoking is not associated with a significantly increased risk of adenocarcinoma of the cervix compared with nonsmokers (squamous cell carcinoma: RR 1.50, 95% CI 1.35-1.66; adenocarcinoma: RR 0.86, 95% CI 0.70-1.05)

Genetic

There is no well-established model of a genetic basis for cervical cancer. Population studies have shown an increased incidence of cervical cancer within families. In the past, such familial clustering had been attributed to shared environmental exposures and risk factors. However, subsequent data comparing full and half siblings have concluded that heritable risk factors far outweigh the shared environmental components. As an example, a Swedish study of over 9000 siblings or half-siblings with cervical cancer or precancer attributed 64 percent of cases to genetics and only 36 percent to environmental exposures.

HPV infections

Investigations are ongoing to identify genetic alterations that may make women less likely to clear persistent HPV infections and more susceptible to the development of cervical cancer.

Findings to-date include an association of cervical cancer with a large variety of polymorphisms
in a wide variety of genes, including those that regulate immunity and susceptibility, cytokine
production ,angiogenesis, tumor suppressor pathways, and signal transducer and activator of
transcription (STAT) pathways .

PATHOGENESIS — Human papillomavirus (HPV) is central to the development of cervical
neoplasia and can be detected in 99.7 percent of cervical cancers. The virology and molecular
pathogenesis of HPV-associated malignancies are discussed in detail separately
There are four major steps in cervical cancer development :
●Oncogenic HPV infection of the metaplastic epithelium at the cervical transformation zone (the
junction between the squamous epithelium of the ectocervix and the glandular epithelium of the
endocervical canal)

● Persistence of the HPV infection

●Progression of a clone of epithelial cells from persistent viral infection to precancer
●Development of carcinoma and invasion through the basement membrane Genital tract HPV infection is extremely common but results in cervical cancer in only a small proportion of infected women. It has been estimated that 75 to 80 percent of sexually active adults will acquire genital tract HPV before the age of 50. The disease burden of genital HPV infection includes conditions other than cervical cancer, including anogenital warts, and cancer of the vulva, vagina, anus, and penis.
Among the more than 40 genital mucosal HPV types identified, approximately 15 are known to be oncogenic .Subtypes HPV 16 and 18 are found in over 70 percent of all cervical cancers.
HPV plays a role primarily in the two most common histologic types of cervical cancer:
squamous cell (69 percent of cervical cancers) and adenocarcinoma (25 percent). The HPV

subtypes associated with squamous cancer are different from those associated with adenocarcinoma. In an international study of over 30,000 cervical cancers, the distribution of HPV subtypes was :
●Squamous cell carcinoma – HPV 16 (59 percent of cases), 18 (13 percent), 58 (5 percent), 33 (5 percent), 45 (4 percent)
●Adenocarcinoma – HPV 16 (36 percent), 18 (37 percent), 45 (5 percent), 31 (2 percent), 33 (2 percent)
Most HPV infections are transient, and the virus alone is not sufficient to cause cervical neoplasia. When HPV infection persists, the time from initial infection to development of high grade cervical intraepithelial neoplasia and, finally, invasive cancer takes an average of 15 years,
although more rapid courses have been reported .

Herpes simplex virus

Herpes simplex virus-2 infection as a cofactor in cervical cancer pathogenesis has been reported in some, but not all studies. Further investigation of this issue is needed.

Prevention

In the first level of prevention there should be avoidance of risk factors, Modifiable Risk Factors are as table 1

Modifiable Risk Factors

Magnitude Risk	*Factor*
Strong (R. R. > 4)	None
Moderate (R. R. 2 – 4).....	Multiple Sexual Partners early age at first intercourse history of S.T.D.
Weak (R. R. < 2).....	Cigarette smoking

Possible(Diet)
- Vegetable – fruit - Vit. C. – Vit. E - Cartenoid
- retinol – Foliate (in some studies)
Alcohol – Fat – Cholesterol – Prot. – Complex Carbohydrate

The population attributable risk means that how much of incidence rate would be decreased if we control the risk factor

In the second level of prevention doing screening is recommended.
The rate of cervical cancer has declined significantly in settings in which cervical cancer screening is employed. In addition, human papilloma virus (HPV) vaccination had been introduced to reduce the incidence of cervical neoplasia.
Cervical cytology as Papa Nicola test is the best specially in developing countries. 5 year survival in insitue stage is near 100% but in invasive stage is only 45%.
Cervical cytology is the principal method for cervical cancer screening. Cytology should also be performed for women with suspected cervical cancer.
Cervical cancer screening, techniques for cervical cytology testing, and interpretation of results are discussed in detail separately.
Human papilloma virus (HPV) testing is used in combination with cervical cytology for cervical cancer screening and helps to determine which women with abnormal cytology results require further evaluation. However, it does not play a role in the diagnosis of malignancy in women with symptoms or a visible lesion suggestive of cervical cancer risk and act in factor with high Population attributable risk (PAR) that is as the table 2

Screening after total hysterectomy is not needed but after subtotal hysterectomy is needed to be continued .
In tired level of prevention rehabilitation and psychological consulting is recommended.

Population attributable risk

FACTOR	*BEST ESTIMATE*	*RANGE*
Two or more sex partners	38%	26 – 50
Cigarette smoking	32%	23 – 41
First intercourse at < 17 years.....	25%	17 -33
Prior genital infection	5%	1 - 50