ESSENTIALS OF CERVICAL CANCER


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ABSTRACT

Cervical cancer is the cancer of cervix, lower portion of uterus. Cervical cancer is a terrible disease that kills 280,000 women every year worldwide, mostly in less developed countries in Africa, Asia and Latin America. Human papillomavirus is the most common cause of cervical cancer. The diagnosis of cervical cancer is done by pap smear test, colposcopy, CT scan, MRI scan etc. The cancer is treated according its stage. In this article an attempt has made to introduce cervical cancer, its risk factors, diagnostic tools, treatments and prevention of cancer.

Keywords: Cancer, Uterus, Cervix, HPV, Radiation, Chemotherapy.

INTRODUCTION

The human body is made up of number of living cells. Normal body cells grow, divide into new cells, and die in an orderly fashion. During the early years of a person's life, normal cells divide faster to allow the person to grow. Cancer begins when cells in a part of the body start to grow out of control. There are many types of cancer, but they occur because of out-of-control growth of abnormal cells. Cancer cell growth is different from normal cell growth. Instead of dying, cancer cells continue to grow and form new, abnormal cells. Cancer cells can also invade other tissues, something that normal cells cannot do.

Cervical cancer is a malignant neoplasm arising from cells originating in the cervix. The cervix is the lower portion of uterus that meets the upper portion of uterus. It is cylindrical in shape and connects the vagina and the uterus. Most cervical cancers are squamous cell carcinomas, observed in the squamous epithelial cells that line the cervix.
Epidemiology
Worldwide, cervical cancer is second most and the fifth deadliest cancer in women. It affects about 16 per 100,000 women per year and kills about 9 per 100,000 per year. Approximately 80% of cervical cancers occur in developing countries Worldwide, in 2008, it was observed that there were 473,000 cases of cervical cancer, and 253,500 deaths per year.

Cervical cancer is the leading cancer among women in terms of incidence rates in 2 out of the 12 Population Based Cancer Registries (PBCRs) in India, and has the second highest incidence rate after breast cancer in the rest of the PBCRs. The age-adjusted incidence is highest in the south, and lowest in Thiruvananthapuram, the capital of Kerela (National Cancer Registry Programme and World Health Organisation). There is a high incidence belt in the north eastern districts of Tamil Nadu.[1]

Causes
The incidence of developing cancer depends on both genetic and non-genetic factors. A genetic factor is hereditary, unchangeable trait and a non-genetic factor is a variable in a person’s environment, which can often be changed. Non-genetic factors may include diet, exercise, or exposure to other substances present in our surroundings. These non-genetic factors are often referred to as environmental factors. Some non-genetic factors can cause the process of healthy cells turn into cancerous.

Human papillomavirus type 16 and 18 are the cause of 75% of cervical cancer. Women who have multiple sexual partners have a greater risk of cancer. Genital warts, is the sign of benign tumor of epithelial cells, are also caused by various strains of HPV. Chlamydia trachomatis is another common sexually transmitted infection.

Human immunodeficiency virus type 1 (HIV-1) and type 2 (HIV-2) are both associated with the development of acquired immunodeficiency syndrome (AIDS). Infection with HIV-1 or HIV-2 may associated with the development of cervical cancer by suppressing the immune system.[2]

Cigarette smoking: Cigarette smoking is one of the cause for an increased risk of developing cervical cancer. There is increased chances of high-risk HPV infections in women who smoke.
Reproductive factors: Among women infected with HPV, risk of cervical cancer increases among women who have had a greater number of full-term pregnancies or a long duration of oral contraceptive use.

Immunosuppression: Women who are taking immunosuppressive medications are at increased risk of developing cervical cells abnormality.

Lower socio-economic status: The incidence of cervical cancer is higher in poor and uneducated women living in rural communities compared to women of higher socioeconomic status.[3]

Long term mental stress: A woman who experiences high levels of stress over a sustained period may be undermining her ability to fight off HPV and be at increased risk of developing cervical cancer it can cause Long-term use of the contraceptive pill slightly raises a woman's risk. [4]

Signs and symptoms
The early stages of cervical cancer may be completely asymptomatic. The presence of malignancy is indicated by vaginal bleeding, contact bleeding, or (rarely) a vaginal mass mass. Also, moderate pain during sexual intercourse and vaginal discharge are symptoms of cervical cancer. In advanced disease, metastases may be present in the abdomen, lungs. Symptoms of advanced cervical cancer may include: loss of appetite, weight loss, fatigue, pelvic pain, back pain, leg pain, swollen legs, heavy bleeding from the vagina, bone fractures, and/or (rarely) leakage of urine or faeces from the vagina.[5,6]

Diagnosis
Visual inspection of the cervix, using acetic acid or Lugol’s iodine to highlight precancerous lesions so they can be seen with the “naked eye”, shifts the identification of precancer from the laboratory to the clinic.[7]

Papanicolaou (Pap) Smear: Routine screening with a Pap smear is used to detect cancerous cells in the cervix early, as well as to detect abnormal cells in the cervix before they become cancerous. In a Pap smear, a sample of cells from the cervix is taken with a small wooden spatula or brush and examined under the microscope. The advantage of the pap smear is that it is relatively cheap and easy to perform. The disadvantages are poor compliance by some women, the high number of false negative smears may be reported, and not all tumours
exfoliate abnormal cells. In place of the conventional Pap test, many women will be tested using a newer type of Pap test that uses a method known as liquid-based cytology. With this method, cervical material that is removed by spatula or brush is rinsed in liquid. The liquid is then processed to separate the cells that are analyzed. These cells are spread in a thin layer on a slide and observed under a microscope.

**Colposcopy**

Colposcopy is the microscopic examination of the cervix. A speculum is inserted into the vagina and the cervix visualised. The cervix is examined by the doctor using a colposcope and it is a low power binocular microscope. The cervix is stained with acetic acid and then iodine which stains any abnormal epithelium. Biopsy or any other appropriate treatment can be performed. This examination does not require a general anaesthetic.[8]

**Biopsy**

As the pap smear is an effective screening test, confirmation of the diagnosis of cervical cancer or pre-cancer needs a biopsy of the cervix. This is done through colposcopy, a magnified visual inspection of the cervix aided by using a dilute acetic acid solution to highlight abnormal cells on the surface of the cervix. Medical devices used for biopsy of the cervix include punch forceps or Spira Brush CX. Colposcopic impression, the estimate of disease severity based on the visual inspection, forms part of the diagnosis. Further diagnostic and treatment procedures are loop electrical excision procedure (LEEP) and conization, in which the inner lining of the cervix is removed and examined pathologically. These are carried out if the biopsy confirms severe cervical intraepithelial neoplasia.

**Examination under anesthetic (EUA)** - The vagina and cervix are examined thoroughly. The patient is under a general anesthetic. The bladder may be checked with a cystoscope, or/and the colon and rectum with a procto-sigmoidoscope to determine whether the cancer has spread. During this whole procedure the doctor may take a biopsy of the bladder, colon/rectum and the lining of the uterus.

**CT (computerized tomography) scan** - a CT scanner emits a series of narrow beams through the human body as it moves through an arc, unlike an X-ray machine which sends just one radiation beam. The final picture is far more detailed than an X-ray one. Inside the CT scanner there is an X-ray detector which can see hundreds of different levels of density. It can see tissues inside a solid organ. This data is transmitted to a computer, which builds up a
3-D cross-sectional picture of the part of the body and displays it on the screen. The doctor will have a much better idea of the size and position of the cancer. The patient will have to have a barium drink beforehand. The barium appears white on the scan. Just before the scan a tampon may be placed into the vagina, and a barium liquid may be placed into the rectum. The whole scan takes from 10 to 30 minutes.

**MRI (magnetic resonance imaging scan)** - an MRI does not use X-rays; it uses magnets and radio waves to build up cross-sectional images of the targeted part of the body. The patient lies very still on a couch inside a long tube which enters a doughnut-like machine. As the machine can become noisy patients will usually be given earphones so that they can listen to music - some may even let you bring your own tunes. All metal items should be removed beforehand because the MRI machine is a powerful magnet. If you have any metal in your body, such as a pacemaker or surgical clips you cannot have an MRI scan. By using high-MRI with a special vaginal coil, a technique to measure the movement of water within tissue, researchers may be able to identify cervical cancer in its early stages.

**Pelvic ultrasound** - this is a device that uses high frequency sound waves which create an image on a monitor of the target area. The patient will be asked to drink plenty of fluids beforehand so that the bladder is full and a clear picture can be viewed. A transvaginal ultrasound device may be inserted into the vagina, or an external device may be placed next to the stomach.[9]

**Pathologic types**

Cervical intraepithelial neoplasia, the precursor to cervical cancer, is often diagnosed on examination of cervical biopsies by a pathologist. Histologic subtypes of invasive cervical carcinoma include the following:\[23]\[24\] Though squamous cell carcinoma is the cervical cancer with the most incidence, the incidence of adenocarcinoma of the cervix has been increasing in recent decades[1].

- Squamous cell carcinoma. (about 80-85%)
- Adenocarcinoma.
- Adenosquamous carcinoma.
- Small cell carcinoma.
- Neuroendocrine carcinoma.

Non-carcinoma malignancies which can rarely occur in the cervix include,
Melanoma.
lymphoma.

Stages of cervical cancer
Cervical cancer is staged by the International Federation of Gynecology and Obstetrics ( FIGO) staging system, which is based on clinical examination, rather than surgical findings. It allows only the following diagnostic tests to be used in determining the stage: palpation, inspection, colposcopy, endocervical curettage, hysteroscopy, cystoscopy, proctoscopy, intravenous urography, and X-ray examination of the lungs and skeleton, and cervical conization.

Stage 0: carcinoma in situ
Even though there are only abnormal cells on the surface layer of the cervix and this is not considered to be part of the cervical cancer staging system. It is not an invasive cancer; the cells have not left the area where they started to grow.

Stage 1: cervical cancer
The cancer is only in the cervix, the neck of the uterus and womb. This stage is divided into:
1A: The cancer can be observed in the microscope only. This stage is further divided into
1A1 - cancer has grown into less than 3 mm of the cervical tissue, and is less than 7 mm wide.
1A2 – cancer growth is 3-5 mm in cervical tissue and is less than 7 mm wide.
1B : cancer is larger and is usually visible with the naked eye, but is confined to the cervical tissue and has not spread. This stage is divided into two:
1B1 - cancer is no larger than 4 cm.
1B2 - cancer is larger than 4 cm.

Stage 2 cervical cancer
The cancer includes the cervix and uterus, but has not yet spread into the pelvic wall or lower portions of the vagina. It is divided into two stages:
2A - the cancer has reached the top of the vagina.
2B - the cancer has reached tissue around the cervix.

Stage 3 cervical cancer
The cancer has spread beyond the cervix and uterus and has reached the surrounding structures of the pelvic area, the lower portion of the vagina, and the pelvic wall (muscles and
ligaments that line the pelvis). The cancer growth may have blocked the ureter (the tube that carries urine from the kidneys to the bladder). It is divided into two stages:

3A - the cancer has reached the lower third of the vagina, but not the pelvic wall.
3B - the cancer has grown through the pelvic wall, or is blocking one ureter or both of them.

The most common treatment option for this stage is a combination of chemotherapy and radiotherapy.

**Stage 4 cervical cancer**
The cancer has spread to nearby organs, such as the bladder or rectum, or it has spread further into other parts of the body, such as the liver, lungs or bones. This is divided into two stages:

4A - the cancer has reached the bladder or rectum.
4B - the cancer has spread further, possibly including the lungs, liver or bones. [10]

**Treatment of cervical cancer**
The choice of treatment depends mainly on the size of the tumor and whether the cancer has spread. Surgery is an option for women with Stage I or II cervical cancer.

**Cone Biopsy**
This is the surgical removal of a cone-shaped segment of the cervix, including both ectocervical and endocervical tissue.

**Lymphadenectomy**
It is the surgical removal of lymph nodes surgically and also known as lymph node dissection (LND), either bilateral or unilateral. In cervical cancer this usually includes the external iliac, internal iliac, common iliac, obturator and presacral nodes.[11]

**Radical hysterectomy**
In a radical hysterectomy or Wertheim’s hysterectomy, the whole uterus is removed together with the upper third of the vagina, parametria and the pelvic lymph nodes with or without the para-aortic nodes. This surgery is associated with bladder dysfunction due to disruption to the nerves during a radical hysterectomy. After surgery, patients are followed up with a limited IV pyelogram to check patency of the ureters.[12]

**Radical trachelectomy**
This surgery involves removing the cervix, together with the top 2-3cms of the vagina and joining the top of the vagina to the lower segment of the uterus. This surgery is used in an
attempt to preserve fertility.[13]

**Radiation therapy**

Radiation therapy uses high-frequency rays to kill cancer cells. It’s an option for women with any stage of cervical cancer. Women with early cervical cancer may choose radiation therapy instead of surgery. It may be used after surgery to destroy any cancer cells that remain in the area. Women with cancer that extends beyond the cervix may have both radiation therapy and chemotherapy.

There are two types of radiation therapy to treat cervical cancer. Some women receive both types:

**External radiation therapy:** A large machine directs radiation at your pelvis or other areas with cancer. The treatment usually is given in a hospital or clinic. You may receive external radiation therapy 5 days a week for several weeks. Each treatment takes only a few minutes.

**Internal radiation therapy** (also called brachytherapy): A narrow cylinder is placed inside your vagina, and a radioactive substance is loaded into the cylinder. Usually, a session of internal radiation therapy lasts only a few minutes. The cylinder and substance are removed, and you can go home. The short session may be repeated two or more times over several weeks. When the radioactive substance is removed, no radioactivity is left in your body. With a less common method of internal radiation therapy, you may stay in the hospital for several days during treatment.

Although radiation therapy is painless, it may cause side effects. The side effects depend mainly on how much radiation is given and which part of your body is treated. Radiation to the abdomen and pelvis may cause nausea, in your genital area. Also, skin on the abdomen and pelvis may become red, dry, and tender.[14]

**Chemotherapy**

The drugs are used to kill cancer cells. For the treatment of cervical cancer, chemotherapy is usually combined with radiation therapy. For cancer that has spread to distant organs, chemotherapy may be used alone. Most drugs for cervical cancer are given intravenously through a thin needle. Some drugs can be taken by mouth. Most women receive chemotherapy in a clinic or at the doctor’s office. Drugs that are swallowed may be taken at home instead. Some patients need to stay in the hospital during treatment.
Drugs Approved to Treat Cervical Cancer
Blenoxane (Bleomycin)
Bleomycin
Cisplatin
Hycamtin (Topotecan Hydrochloride)
Platinol (Cisplatin)
Platinol-AQ (Cisplatin)
Topotecan Hydrochloride.

The side effects depend mainly on which drugs are given and how much. Chemotherapy kills fast-growing cancer cells, but the drugs can also harm normal cells that divide rapidly.[15] Blood cells: When chemotherapy lowers the levels of healthy blood cells, you’re more likely to get infections, bruise or bleed easily, and feel very weak and tired. Your health care team will check for low levels of blood cells. If the levels are low, your health care team may stop the chemotherapy for a while or reduce the dose of drug. They may also give you medicines that can help your body make new blood cells.

Cells in hair roots: Chemotherapy may cause hair loss. If you lose your hair, it will grow back, but it may change in color and texture.

Cells that line the digestive tract: Chemotherapy can cause a poor appetite, nausea and vomiting, diarrhea, or mouth and lip sores.

Other side effects include skin rash, tingling or numbness in your hands and feet, hearing problems, loss of balance, joint pain, or swollen legs and feet.

Complications associated with cervical cancer
- Fistulae
A fistula is an abnormal opening between epithelial surfaces. In cervical cancers, three types of fistula may occur:
vesicovaginal (between bladder and vagina)
ureterovaginal (between ureter and vagina)
rectovaginal (between rectum and vagina)
The first two are more common and are related to surgery. The latter is less common and usually related to pelvic radiation.
• Lymphoedema
The lymphoedema can arise if the lymph nodes are removed by surgery or damaged by radiotherapy which can occur after the treatment for cancer. Lymphoedema may occur in the legs if pelvic nodes are removed in the treatment for cervical cancer.

• Ureteric Compression & Stents
Ureteric compression is another potential complication of advanced cervical carcinoma and is usually caused by progressive tumour. Ureteric compression may be diagnosed by: biochemical studies i.e. an elevated serum creatinine and decreased urinary output. Treatment is often insertion of a ureteric stent (typically a double-J or pigtail stent) usually inserted via a cystoscopy but can be by open surgery.[16]

Survival rate of cervical cancer
The survival rate for women with early diagnosed cervical cancer after five years is high.[17]

<table>
<thead>
<tr>
<th>Stage</th>
<th>Five year survival (approx %)</th>
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<tbody>
<tr>
<td>1A</td>
<td>98</td>
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<tr>
<td>1B</td>
<td>95</td>
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<tr>
<td>2A</td>
<td>75</td>
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<td>2B</td>
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<td>3A</td>
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<td>10</td>
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Prevention of cervical cancer

Health Promotion & Education
According to a WHO report on comprehensive cervical cancer control, health education and promotion should be an integral part of any national cervical cancer control programme (WHO, 2006). It should incorporate an awareness component, informing women and/or their families:
• that cervical cancer is preventable,
• about the signs and symptoms of the disease,
• what they should do if signs and symptoms are present,
• that regular screening is essential to detect the cancer early and avoid disability and death from the disease.
Screening
The widespread introduction of cervical screening by the Papanicolaou test, or Pap smear for cervical cancer has been credited with dramatically reducing the incidence and mortality of cervical cancer in developed countries. Pap smear screening every 3–5 years with appropriate follow-up can reduce cervical cancer incidence by up to 80%. Abnormal results may suggest the presence of precancerous changes allowing examination and possible preventive treatment. If precancerous disease or cervical cancer is detected early, it can be monitored or treated relatively noninvasively, with little impairment of fertility.

Cervical cancer screening is typically recommended starting at age 21. Recommendations for how often a Pap smear should be done vary from once a year to once every five years, in the absence of abnormal results. Guidelines vary on how long to continue screening, but well-screened women who have not had abnormal smears can stop screening about age 60 to 70. Liquid-based cytology is another potential screening method. Although it was probably intended to improve on the accuracy of the Pap test, its main advantage has been to reduce the number of inadequate smears from around 9% to around 1%. This reduces the need to recall women for a further smear.[18]

Vaccination
There are two HPV vaccines which reduce the risk of cancerous or precancerous changes of the cervix and perineum by about 93%.

HPV vaccines are typically given to women age 9 to 26 as the vaccine is only effective if given before infection occurs. The vaccines can be effective for at least 4 to 6 years, and it is believed they will be effective for longer; however, the duration of effectiveness and whether a booster will be needed is unknown. The high cost of this vaccine has been a cause for concern. Several countries have considered programs to fund HPV vaccination.[19]

Drugs Approved to Prevent Cervical Cancer
Cervarix (Recombinant HPV Bivalent Vaccine)
Gardasil (Recombinant HPV Quadrivalent Vaccine)
Recombinant Human Papillomavirus (HPV) Bivalent Vaccine
Recombinant Human Papillomavirus (HPV) Quadrivalent Vaccine
**Condoms**- Condoms are one of the way to offer some protection against cervical cancer. Evidence on whether condoms protect against HPV infection is mixed, but they may protect against genital warts and the precursors to cervical cancer. They also provide protection against other STDs, such as HIV and Chlamydia, which are associated with greater risks of developing cervical cancer. Condoms may also be useful in treating potentially precancerous changes in the cervix. [20]

**Nutrition**- Vitamin A is associated with a lower risk as is vitamin B12, vitamin C, vitamin E, and β-carotene. [21]

**Cervical Cancer Research Programs**
There are several cervical cancer research programmes implemented in India. The National Cancer Registry Programme (NCRP), established by the Indian Council of Medical Research (ICMR) acts as a surveillance system for cancer in India. Under the NCRP, Population Based Cancer Registries (PBCRs) have been established at 19 locations (Mizoram, Sikkim, Imphal, Kamrup, Silchar, Dibrugarh, Bangalore, Chennai, Mumbai, Delhi, Bhopal, Ahmedabad, Nagpur, Kolkata, Aurangabad, Pune, Kollam, Thiruvananthapuram and Barshi) and Hospital Based Cancer Registries (HBCRs) have been initiated at Dibrugarh, Chandigarh, Thiruvananthapuram, Bangalore and Mumbai. The PBCRs collect data on cancer incidence and mortality. The HBCRs collect data on cancer patterns, and also gather information on care of patients, treatment options, and helps in patient follow up. Another most promising cervical cancer research study in India is a clinical trial, being funded by the IARC, with the aim of assessing whether a two dose HPV vaccine would confer similar protection against the infection relative to a three dose vaccine. The estimated completion date has been given as May 2014.[22]

**CONCLUSION**
Cervical cancer is one of the fatal diseases now a day. It can be cured completely by the treatment and can avoid the risk of it by taking the prevention on time like vaccination. There are various drugs available to fight with cancer. The social awareness about health is also necessary.
REFERENCES


