CERVICAL CANCER: Pathogenesis, Risk Factors, Diagnosis and Treatment

Vaibhavi P Pandhare¹*, Divya R Bramhankar², Nikita E Nikam³, Ramkrushna M Nikam⁴, Pooja Mairal⁵

Abstract-
Cervical cancer is 4th most common cancer among women which causes death. This cancer is observe in cervix which is entrance to uterus from vagina human papilloma virus (HPV) is most common risk factor which is transmitted sexually. Most infection of HPV causes no symptoms. Tenacious infection causes cancer. Screening and vaccination are the best method to avoid HPV infections. According to WHO, in 2018 570000 women worldwide war diagnosed with cervical cancer and about 311000 were died.

Keywords- cervical cancer, human papilloma virus, vaccine, women, infection

Introduction-
Cervical cancer is the fifth most common cancer among humans where 4th most common cancer in women. Cervical cancer developed in women's cervix which is the entrance to uterus from vagina. The causative factor of Cancer is human papilloma virus (HPV) it is transmitted through sexual contact. In 2018, about 570000 women diagnosed with cervical cancer among which 3,11,000 women died. In India approximately 132000 new cases of cancer are currently diagnosed and 74000 deaths are occurred.
Human Papilloma Virus-

Papilloma viruses are species-specific and infect squamous epithelia and mucus membrane. Human papilloma virus can infect only humans. Over 82 types of HPV are recognized. HPV is a group of more than 200 viruses which are related to each other. High risk of HPV types including 16, 18, 31, 33, 35, 45, 51, 52, 56, 58, 59, 66 and 68. HPV16 and HPV18 are the most common HPV causes cervical cancer. HPV can infect both males and females. HPV infects cells present in cervix, oropharynx, anus, penis, vagina and vulva. It infects squamous cells which are present in the inner surface of organs.

Pathogenesis-

HPV infection causes to basal cell of stratified epithelium. Both cell-mediated immunity & antibody which induced by infection can cause regression of warts. Patients such as having AIDS & HIV infected women have high risk of carcinoma.

Infection mechanism of HPV-

HPV integrate into host DNA -- expression of viral protein E6 & E7
Viral protein activates cyclin A & E -- permits further cell proliferation

CERVICAL CANCER

Normal (front view) - Early stage IB - Late stage IB - Stage IIB
Uterus - Cancer tissue - Bleeding
Cervix - Cancer tissue - The cancer spreads outside cervix
Vagina - Cancer tissue - Bleeding
Healthy cervix (viewed from below) - Carcinoma only in cervix
Risk factors-

1) Many sexual partners
2) Early sexual activity (< 16 year old)
3) Other sexually transmitted infections
4) Weakend immune system
5) Smoking
6) Exposure to miscarriage prevention drug
7) Low socio-economic level
8) Early marriage
9) Early childbirth
10) Having cervicitis
11) Poor menstrual hygiene

Signs and symptoms-

1) Vaginal bleeding after intercourse
2) Watery, bloody vaginal discharge that have foul odour
3) Pelvic pain
4) Pain during intercourse
5) Swollen glands

Usually having no symptoms. Precancerous lesions may cause itching or bleeding.

Types of cervical cancer-

1) Squamous cell carcinoma

This type of cancer is observed in thin, flat squamous cell of outer part of cervix. Most of cervical cancers are found to be of this type.
2) Adenocarcinoma

This type of cancer is observed in column shaped glandular cells present in cervical canal.

**Diagnosis**

Evaluations of cancerous cervical lesions are important for diagnosis of cervical cancer. Most of cervical cancer are asymptomatic, hence overt mass in early stages are not present. Diagnosis involves testing and evaluation of symptoms. To finalize the diagnosis, diagnostic biopsy is needed.

1) Pap smear test- used to screen cervical cancer
2) Biopsy- a small piece of tissue is taken
3) Colposcopy
4) Cone biopsy
5) LLETZ
6) Blood test
7) Computerized tomography scan
8) Pelvic ultrasound

**Treatment**

Precancerous lesions are cured in women who are younger than 25 years. Colposcopy used to evaluate abnormal lesions which can leads to cancer. Low-risk lesions are watched and reevaluated. High risk lesions are treated on the basis of size and location. Cryotherapy is used to treat precancerous lesions. conization, laser or Loop Electrosurgical Excision Procedure (LEEP) used to manage lesions present in endocervical canal. Stagging based on findings, results from examination imaging, reported signs and symptoms. Grading used to find size and depth of cancer. For treatment of early stage of infection, radical hysterectomy is used. After hysterectomy, chemotherapy and radiation are the next treatment to slow the rate of growth of cancer.

**Prevention**

1) Vaccination

Receive vaccine to prevent HPV infection. It may reduce risk of cervical cancer and other HPV related cancers.

2) Routine Pap test

pap test used to detect precancerous lesions. Routine Pap test should be started at age 21.

3) Practice safe sex
Take preventive measures about sexually transmitted diseases such as using condom and limiting number of sexual partners.

4) Don't smoke
5) Diet

Take vitamin A and vitamin C rich food in daily diet.

**HPV vaccine**

Vaccine provide protection to women who are not exposed to HPV. Vaccine is not used to treat HPV infection. Vaccine gives protection at ages 9 to 12 years. Vaccination prevent up to 90% of HPV related cancer. Vaccine is given in 3 doses for 6 months. Vaccine is intramuscular (IM) injection given in deltoid muscles of upper arms. Vaccine is recommended for girls and boys at age 11 or 12 years and for adults at age of 27 and 45. Vaccination is recommended by Centre for Disease Control and preventions (CDC)'s Advisory Committee on Immunization Practices (ACIP) to avoid HPV infection.

**Types of HPV vaccine**

Globally licensed two vaccines are available in India. These are Gardasil and cervix produced by Recombinant DNA technology. Gardasil is a quadrivalent vaccine marketed by Merck. It is mixture of L1 protein of HPV serotypes 16, 18, 6 and 11. This vaccine protect against both cervical cancer and genital warts. Cervix is bivalent vaccine marketed by Glaxo Smith Kline. It is mixture of L1 protein of HPV serotype 16 and 18. This vaccine product is against only cervical cancer.
Reference-


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