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Human Pappilioma Virus and Sexually Transmitted Disease

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Abstract: ***Cervical cancer still remains the most common cancer affecting the Indian women. India alone contributes 25.41% and 26.48% of the global burden of cervical cancer cases and mortality, respectively. Ironically, unlike most other cancers, cervical cancer can be prevented through screening by identifying and treating the precancerous lesions, any time during the course of its long natural history, thus preventing the potential progression to cervical carcinoma. Several screening methods, both traditional and newer technologies, are available to screen women for cervical precancers and cancers. No screening test is perfect and hence the choice of screening test will depend on the setting where it is to be used. Similarly, various methods are available for treatment of cervical precancers and the selection will depend on the cost, morbidity, requirement of reliable biopsy specimens, resources available, etc. The recommendations of screening for cervical cancer in the Indian scenario are discussed.***

Keywords: cervical cancer, human pallioma virus, sexually transmitted disease

1. Introduction

Cervical cancer is the second commonest cause of cancer among women. According to the World Health Organization (WHO) data, in 2006 there were 1.4 million women who were suffering from cervical cancer and 80% of deaths among them were of women from developing countries. Genital infection with Human Papilloma Virus (HPV) is one of the major etiological factors for developing cervical cancers in almost all countries (World Health Organization, 2005). Papilloma viruses were first identified cloned and sequenced from cervical tumor specimens and were subsequently established as important causative agents for the development of cervical cancer. Differences in prevalence rates are observed worldwide. Infection is more common in sexually active young women of 18-30 years and a reduction in acquisition of infection is observed after 30 years.

Human Papilloma Virus

Papilloma viruses are small non-enveloped icosahedral viruses of approximately 50–60 nm in diameter. It contains a circular, double-stranded DNA genome (7000–8000 bp) that exists in a chromatinized state. All Papilloma viruses belong to the Papillomaviridae family, which includes 16 different genera. It is divided into four major genus levels known as alpha, beta, gamma and delta (According to a phylogenetic analysis among the sequences of 118 Papilloma virus types). The alpha genus contains the viruses associated with the development of mucosal tumors in humans. The beta genus is associated with the development of cutaneous tumors. HPV group of viruses include more than 80 different types associated with a variety of epidermal warts and skin lesions and some of which are associated with skin cancer. Low risk HPV subtypes (Type 6, 11) are associated with more benign skin lesions such as warts (papillomas). High-risk subtypes (Type 16, 18) can cause neoplasia (abnormal cell growth) or dysplasias and are associated with the development of cervical and anal cancers.

Life cycle of the virus

The life cycle of the virus is divided into four main steps known as entry, establishment of the non-productive infectious state, Maintenance of the non-productive infectious state and Productive stage. HPVs are specifically epitheliotropic and their life cycle takes place within stratified squamous epithelia. Subsequent steps in the life cycle of the virus can be divided into four stages:

Entry-Entry is established that HPVs initiate infection by penetrating through micro traumas in the epithelial to reach the basal cells, which are believed to be the target cells for HPV infection. The mechanism for virus entry into the basal cells is not entirely understood.

Establishment-The non-productive infectious state is once HPV particle enters the host cell, the virus relies primarily on the host's cellular machinery to replicate the virus DNA. The HPV genome becomes established as a low copy number nuclear plasmid inside in the infected basal cells. Within these cells, only early viral gene products are expressed and consequently referred as the non-productive stage of infection

Maintenance-The non-productive infectious state is a hallmark of HPV infection. It is a prerequisite for the development of cancer. It requires that the viral genome be maintained over multiple cell divisions. But the mechanism is still unclear.

Production-It begins when the daughter cells derived from the infected basal cells. It starts to differentiate. The virus delays the terminal differentiation programme of the cell. It redirects the cell's DNA replicative capacity. Then it allows amplification of the viral genome and expression of the late viral genes which are necessary for the production of progeny virus and subsequent viral release

Factors Contributing to Cervical Cancer

There are several factors which contribute to facilitate HPV infection which leads to the formation of cancer. Some of

those factors are tobacco smoking, parity fertility and oral contraceptive use. Immunosuppression and certain dietary deficiencies are other probable cofactors for the infection. The potential risk of infection from non penetrative sexual contact remains undetermined but there is a possible association between oral and penile contact and oral HPV which leads to oral cancer. HPV coinfection with HIV has also been identified as an established cofactor which increases the risk of cancer and HPV coinfection with Chlamydia trachomatis and Herpes simplex virus 2. The biological factors are genetic and immunological host factors and viral factors are the virus type, variants of type, viral load and viral integration. Those are important factors but have not been clearly identified the exact mechanism behind those factor the several HPV infections have been described.

Anogenital warts
Anogenital warts (AGWs) are the most common clinical manifestation of HPV infection. It is mainly caused with HPV 6 and 11 and highly infectious. An estimated 65 percent of people whose sexual partner has genital warts will develop warts themselves.

Cervical and Anal cancer
The anal cancer in men appears to be increased when it is compared with women. Beside other human behaviors receptive anal intercourse and HIV infection were the most important risk factors for anal cancer.

Penile cancer
The major risk factors for penile cancer are lack of male Circumcision (MC), poor genital hygiene, AGWs and HIV infection. Other risk factors for penile cancer that have been reported are smoking, early age of first sexual intercourse, high lifetime number of female sexual partners, lack of condom use, chronic inflammatory conditions.

Cancer of vagina Vaginal cancer is a less frequent cancer in women.

Ovarian cancer There is an increased risk of ovarian cancer in older women and in those who have a first or second degree relative with the disease.

Cancer of urinary bladder
The most significant risk factor associated with bladder cancer is smoking.

Non sexually transmitted HPV infection (Nongenital warts)
It is the most common warts on hands, fingers and knees. There are two types of warts which have been observed among the general population, known as planter warts and flat warts. Basically planter warts can be seen on feet and flat warts can be seen on hands and faces.

Cancer of eye
The HPV could be transmitted in utero during vaginal delivery.

Nasopharyngeal carcinoma (NPC)
Nasopharyngeal cancer is an uncontrolled growth of cells that begins in the nasopharynx, the passageway at the back of the nose.

Other Cancers

Cancer of lung: There are several reports on the association of HPV infection with lung cancer which are rare but also controversial. The formation of the lung cancer can occur due to HPV 18.

Cancer of Esophagous The most important reasons for the infection are different food habits, smoking and tobacco chewing. Ethnicity showed a significant difference in the frequency of HPV infection.

Diagnosis of Cervical Cancer:

The following tests may be used to diagnose cervical cancer:

- **Bimanual pelvic examination and sterile speculum examination.** In this examination, the doctor will check for any unusual changes in the patient's cervix, uterus, vagina, ovaries, and other nearby organs. A Pap test is often done at the same time. Some of the nearby organs are not visible during this exam, so the doctor will insert 2 fingers of 1 hand inside the vagina while the other hand gently presses on the lower abdomen to feel the uterus and ovaries. This exam typically takes a few minutes and is done in an examination room at the doctor’s office.
- **Pap test.** During a **Pap test**, the doctor gently scrapes the outside and inside of the cervix, taking samples of cells for testing.

The liquid-based cytology test often referred to as ThinPrep or SurePath, transfers a thin layer of cells onto a slide after removing blood or mucus from the sample. The sample is preserved so other tests can be done at the same time, such as the HPV test.

Computer screening, often called AutoPap or FocalPoint, uses a computer to scan the sample for abnormal cells.

HPV typing test: An HPV test is similar to a Pap test. The test is done on a sample of cells from the cervix. The doctor may test for HPV at the same time as a Pap test or after Pap test results show abnormal changes to the cervix.

Colposcopy: The doctor may do a **colposcopy** to check the cervix for abnormal areas. Colposcopy can also be used to help guide a biopsy of the cervix. During a colposcopy, a special instrument called a colposcope is used. The colposcope magnifies the cells of the cervix and vagina, similar to a microscope. It gives the doctor a lighted, magnified view of the tissues of the vagina and the cervix. The colposcope is not inserted into the body, and the examination is similar to a speculum examination. It can be done in the doctor's office and has no side effects. It can also be done on pregnant women.

Biopsy: A **biopsy** is the removal of a small amount of tissue for examination under a microscope. Other tests can suggest that cancer is present, but only a biopsy can make a definite

diagnosis. A pathologist then analyzes the sample (s). A pathologist is a doctor who specializes in interpreting laboratory tests and evaluating cells, tissues, and organs to diagnose disease. If the lesion is small, the doctor may remove all of it during the biopsy.

Other types of biopsies include:

Endocervical curettage (ECC): If the doctor wants to check an area inside the opening of the cervix that cannot be seen during a colposcopy, they will use ECC. During this procedure, the doctor uses a small, spoon-shaped instrument called a curette to scrape a small amount of tissue from inside the cervical opening.

Loop electrosurgical excision procedure (LEEP): LEEP uses an electrical current passed through a thin wire hook. The hook removes tissue for examination in the laboratory. A LEEP may also be used to remove a precancer or an early-stage cancer.

Conization (a cone biopsy): This removes a cone-shaped piece of tissue from the cervix. Conization may be done as treatment to remove a precancer or an early-stage cancer. It is done under a general or local anesthetic and may be done in the doctor's office or the hospital.

If the biopsy shows that cervical cancer is present, the doctor will refer you to a gynecologic oncologist, which is a doctor who specializes in treating this type of cancer. The specialist may suggest additional tests to see if the cancer has spread beyond the cervix.

Pelvic examination under anesthesia: In cases where it is necessary for treatment planning, the specialist may re-examine the pelvic area while the patient is under anesthesia to see if the cancer has spread to any organs near the cervix, including the uterus, vagina, bladder, or rectum.

X – ray: An x-ray is a way to create a picture of the structures inside of the body using a small amount of radiation. An intravenous urography is a type of x-ray that is used to view the kidneys and bladder.

Computed tomography (CT or CAT) scan: A **CT scan** takes pictures of the inside of the body using x-rays taken from different angles. A computer combines these pictures into a detailed, 3-dimensional image that shows any abnormalities or tumors. A CT scan can be used to measure the tumor's size. Sometimes, a special dye called a contrast medium is given before the scan to provide better detail on the image. This dye can be injected into a patient's vein or given as a pill or liquid to swallow.

Magnetic resonance imaging (MRI): An **MRI** uses magnetic fields, not x-rays, to produce detailed images of the body. MRI can be used to measure the tumor's size. A special dye called a contrast medium is given before the scan to create a clearer picture. This dye can be injected into a patient's vein or given as a pill or liquid to swallow.

- **Positron emission tomography (PET) or PET-CT scan.** A PET scan is usually combined with a CT scan (see above), called a **PET-CT scan**. A PET scan is a way to create pictures of organs and tissues inside the body. A small amount of a radioactive sugar substance is injected into the patient's body. This sugar substance is taken up by cells that use the most energy. Because cancer tends to use energy actively, it absorbs more of the radioactive substance. A scanner then detects this substance to produce images of the inside of the body.
- **Molecular testing of the tumor.** Your doctor may recommend running laboratory tests on a tumor to identify specific genes, proteins, and other factors unique to the tumor. If there are signs or symptoms of bladder or rectal problems, these procedures may be recommended and may be performed at the same time as a pelvic examination:
- **Cystoscopy.** A **cystoscopy** is a procedure that allows the doctor to view the inside of the bladder and urethra (the canal that carries urine from the bladder) with a thin, lighted tube called a cystoscope. The person may be sedated as the tube is inserted in the urethra. A cystoscopy is used to determine whether cancer has spread to the bladder.
- **Sigmoidoscopy (also called a proctoscopy).** A **sigmoidoscopy** is a procedure that allows the doctor to see the colon and rectum with a thin, lighted, flexible tube called a sigmoidoscope. The person may be sedated as the tube is inserted in the rectum. A sigmoidoscopy is used to see if the cancer has spread to the rectum.

2. Treatments

Genital warts can be treated by a doctor and by different methods. All treatment involves destroying the patient's skin which has grown in a strange and annoying way.

Podofilox gel: A patient-applied treatment for external genital warts.

Imiquimod cream: A patient-applied treatment. Chemical treatments (including trichloracetic acid and podophyllin), which must be applied by a trained health care provider to destroy warts.

Electrosurgery: Uses and electric current to burn off the warts.

Interferon: An antiviral drug, which can be injected directly into warts.

Laser therapy: Lasers are simply very intense light sources. This light has an enormous amount of energy that heats the tissue enough that it vaporizes. .

Cryotherapy: Liquid nitrogen or cryotherapy is used to deep freeze the wart tissue. It uses liquid nitrogen which is applied to the wart, the water in the cells expands, thus exploding the infected tissue. The exploded cells can no longer hide the human Papilloma virus from the body's immune system. The immune system then works to destroy the virus particles Periungual area may scar if cryotherapy with liquid nitrogen is used improperly. Scarring could lead to permanent nail disfiguration

Adhesive tape therapy: Place several layers of waterproof adhesive tape over the wart region. Tape doesn't r remove for 6-1/2 days. Then take off the tape and open the area to the air for 12 hours. Then reapply tape for another 6-1/2 days. The tape works best in the region around the fingernail, because the air tight, moist environment under the tape does not allow the virus to grow and reproduce.

Salicylic acid therapy: Salicylic acid is stored either as a liquid to paint on the wart or as a plaster to be cut out and placed on the wart tissue. The area with the wart should be soaked in warm water for 5-10 minutes. The wart should then be pared down with a simple razor and then should be discarded. It doesn't shave far enough to make the wart bleed. Apply the salicylic acid preparation to the wart tissue. It shouldn't touch the other areas of the skin because of salicylic acid's potential to injure normal tissue.

Prevention of HPV-Associated Infection and Disease in Women and Men

HPV Vaccines: Vaccines are the ideal form of primary prevention for infectious diseases and have been successful in the control of many other infectious diseases. . HPV vaccines are very effective at preventing infection and disease related to the vaccine-specific genotypes in women with no evidence of past or current HPV infection. Protection lasts for at least 5 years. HPV vaccines will reduce the risk of cervical cancer. But it doesn't eliminate the risk of a cancer. The screening programmes are very useful and more important interventions for cervical cancers

3. Awareness of Cervical Cancer

The estimation of HPV and cervical cancer cases is most likely an underestimation of the true incidence of the disease due to a low number of cervical screening facilities and lack of a national cancer registry. The limited availability of cervical screening, lack of accurate knowledge and awareness of cervical cancer is resulting for the increasing number of cervical cancer cases. Over 80% of the cervical cancer cases diagnosed at an advanced clinical stage which often have a very poor prognosis. Women from both city and rural areas are found to have a low knowledge and awareness of cervical cancer, HPV and the HPV vaccine. Awareness of cervical cancer is positively associated with having knowledge in STIs, formal education on sexual behavior, current contraception use and having an abortion. Both men and women have been given the knowledge of STIs and formal education by using health literacy through awareness programmes.

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