ASSOCIATION OF HPV INFECTION IN WOMEN WITH ABNORMAL CERVICAL CYTOLOGY IN GOVT. RAJAJI HOSPITAL, MADURAI

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CERTIFICATE

This is to certify that the dissertation entitled **"ASSOCIATION OF HPV INFECTION IN WOMEN WITH ABNORMAL CERVICAL CYTOLOGY IN GOVT RAJAJI HOSPITAL, MADURAI** " is a bonafide work done by Dr.ASHWINILAKSHMI .T.S. in the institute of Madurai medical college , Madurai in partial fulfilment of the university rules and regulations for ward of MS degree in Obstetrics and Gynaecology under my guidance and supervision during the academic year 2019-2020.

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DECLARATION

I, **DR ASHWINILAKSHMI.T.S.** solemnly declare that this dissertation entitled **"ASSOCIATION OF HPV INFECTION IN WOMEN WITH ABNORMAL CERVICAL CYTOLOGY IN GOVT RAJAJI HOSPITAL, MADURAI "** was done by me at the Department of Obstetrics and Gynaecology, Govt. Rajaji Hospital, Madurai medical college, Madurai during 2019-2020 under the guidance and supervision of **Prof. DR.N.SUMATHI M.D, DGO.,** This dissertation is submitted to the Tamil Nadu Dr.M.G.R Medical University towards the partial fulfilment of requirements for the award of M.S Degree in Obstetrics and Gynaecology (Branch III)

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ABBREVATIONS

1.HPV	Human Papilloma Virus
2.HSIL	High grade Squamous Intraepithelial Lesion
3.LSIL	Low grade Squamous Intraepithelial Lesion
4.ASC	Atypical Squamous Cells
5.ASCUS	Atypical Squamous Cells of Undetermined Significance
6.ASC-H	Atypical Squamous Cells suspicious for HSIL
7.NILM	Negatuive for Intraepithelial Lesion or Malignancy
8.DNA	De-oxy ribo Nucleic Acid
9.PCR	Polymerase Chain Reaction
10.ACS	American Cancer Society
11.ACOG	American College of Obstertricians & Gynecology
12.CIN	Cervical Intraepithelial Neoplasia
13.ICC	Invasive Cervical Cancer
14.HIV	Human Immuno deficiency Virus

CONTENTS

ASSOCIATION OF HPV INFECTION IN WOMEN WITH ABNORMAL CERVICAL CYTOLOGY

INTRODUCTION

INTRODUCTION

"Cancer is a word, not a sentence."

- John Diamond

Cervical cancer is the world's second most frequent cancer. Cervical malignancies account for 9% of all new cancer cases, with India bearing 20%–30% of the burden. Furthermore, India is responsible for 77,100 of all cervical cancer-related deaths. **(Nisha Madaan et al., 2019)[1]**

Human papillomavirus, a double-strand DNA virus, causes cervical cancer. It is the fourth most prevalent malignancy in women worldwide. Human papillomavirus (HPV) infections have been linked to nearly all of the 500,000 occurrences of invasive cervical cancer (ICC) that occur each year around the world. **(H.J. Alotaibi et al., 2020)[2]**

There are 110 different varieties of HPV infections, although only half of them infect the vaginal tract. Only 13 varieties are carcinogenic, according to the IARC WHO classification, while the remaining 7 are possibly carcinogenic. HPV-16, 18, 31, 33, 35, 52, 56, 39, 45, 51, 58, 59, and 68 are carcinogenic and have been linked to cervical intraepithelial lesions, which can lead to cervical cancer. **(Sunita Malik et al., 2019)[3]**

Persistent infection with high-risk HPVs in the cervix can cause cytological abnormalities, which can lead to premalignant lesions such as low-grade squamous intraepithelial lesion and high-grade squamous intraepithelial lesion, which can progress to malignancy. Chlamydia spp., trichomonas vaginalis (TV), herpes simplex virus (HSV), and bacterial vaginosis (BV) are

among the sexually transmitted infections (STIs) that may play a role in cervical carcinogenesis. **(Gangotree Mohanty et al., 2021)[4]**

The single most important predictor related with invasive cervical cancer is never or seldom being checked for cervical cancer. Immunosuppression from any source, including human immunodeficiency virus infection, smoking, co-infection with other sexually transmitted infections, parity, prolonged use of oral contraceptives, and diet all enhance HPV persistence and the risk of invasive cervical cancer. **(Lilach Leibenson et al., 2011)[5]** Primary prevention consists of HPV vaccine, while secondary prevention consists of effective HPV testing and screenings to treat cervical precancerous lesions. **(Ping Li et al., 2021)[6]**

Cervical cancer treatment options include radical hysterectomy, radiation, chemotherapy, and concurrent chemo-radiotherapy. Despite the multitude of treatment methods available, tumor recurrence rates range from 10% to 50%, with a 5-year survival rate of around 65 percent depending on the stage of the disease. Human papillomavirus infection screening tests typically contain 13 high-risk Human papillomavirus (HR-HPV) genotypes, with Human papillomavirus - 16, 33, 45, 18, 31, 52, and 58 genotypes considered to be responsible for more than 90% of cervical cancer cases. The most recent US cervical cancer screening recommendation proposes a screening system based on age, with no screening advised for women under 21 or over 65, cytology alone every three years for women 21–29 years, and cytology with HR-HPV testing for women 30–65 years. Cervical cancer screening to detect early-stage lesions has resulted in significant decreases in cervical cancer incidence and mortality. **(Fang Liu et al., 2021)[7]**

The aim of the study is to determine the association of Human papillomavirus infection in women with abnormal cervical cytology.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

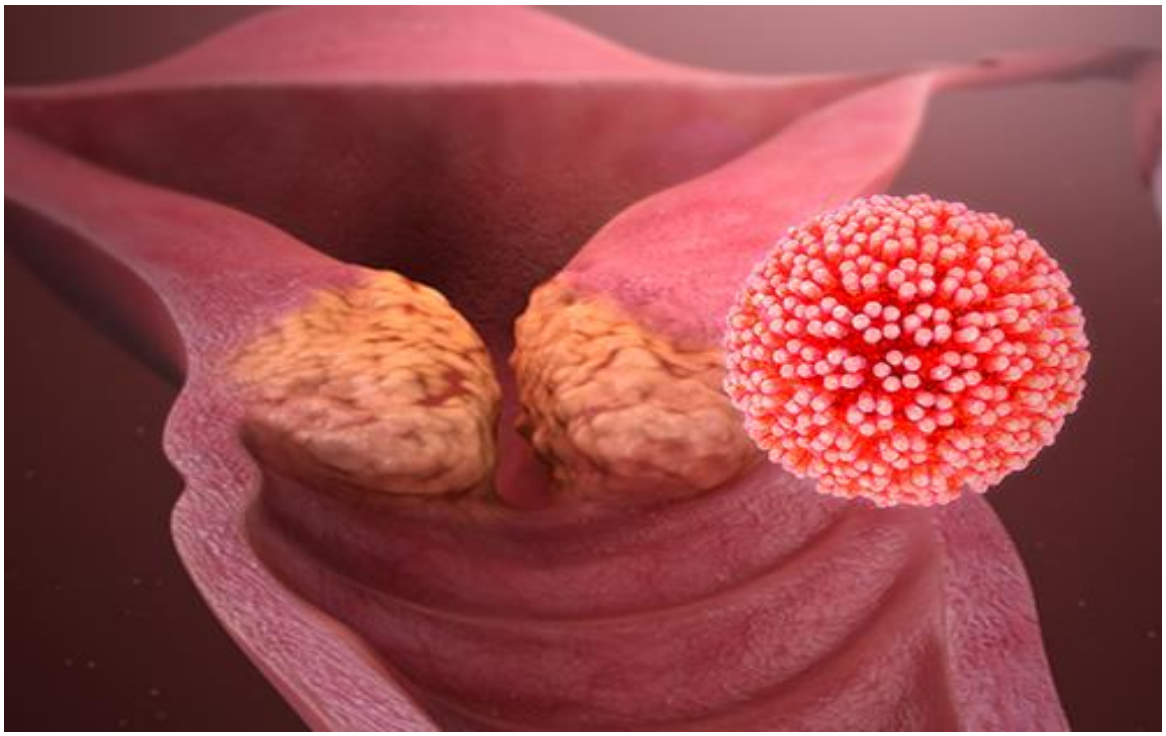
Human Papillomavirus infection

The most major risk factor for cervical cancer is infection with the human papillomavirus (HPV). Human papillomavirus causes papillomas, also known as warts, which are a form of growth caused by the virus. **(American cancer society -Cervical Cancer Risk Factors, 2021)[8].** Human papillomavirus is a virus that is spread from person to person by skin-to-skin contact. There are more than 100 different types of Human papillomavirus more than 40 of them being transmitted through sexual contact and affecting mouth, genitals, and throat. **(Alana Biggers and Amber Erickson, 2021)[9]** It can cause cancers, including cancer of the cervix, vagina, vulva, penis and anus, and some head and neck cancers. **(Human papillomavirus Australian Government Department of Health, 2021)[10]**

Human papillomavirus is a double-stranded, non- enveloped, circular DNA virus that causes a variety of epithelial lesions and malignancies. It can cause cutaneous and anogenital warts, which can proceed to cancer depending on the subtype. The Human Papillomavirus causes a variety of epithelial diseases and malignancies, mostly on the cutaneous and mucosal surfaces. **(Lynette Luria and Gabriella Cardoza-Favarato, 2021)[11]**

Human papillomavirus infections are asymptomatic in two-thirds of cases. High-risk Human papillomavirus varieties, on the other hand, can cause variety of precancerous and cancerous lesions, including cervical cancer. Furthermore, Human papillomavirus infections are linked to a variety of cancers that can affect men. Ano-genital warts (condyloma) are common in both men and women and can be caused by low-risk Human papillomavirus. **(Emilien Jeannot et al., 2019)[12]**

Figure 1: Human papillomavirus



Source: Human papillomavirus, topdoctors, 2021[13]

The majority of infections are harmless, resulting in cutaneous warts on the feet, hands, and anogenital regions. Warts are keratin-filled hypertrophied skin patches that are mostly a cosmetic annoyance; they usually disappear on their own after 1–5 years. Only a small percentage of Human papillomavirus infections persist and proceed to cancer, such as oropharyngeal, vulvar, cervical, vaginal, and penile cancer. **(Kehinde Sharafadeen Okunade, 2019)**[14]

Types of Human papillomaviruses

The human papillomavirus is DNA tumor virus promotes epithelial growth on the skin and mucosa. There are around 100 different strains of the virus, with about 30 to 40 of them

infecting the human genital tract. Oncogenic or high-risk kinds (16, 18, 39, 45, 31, 33, 35, 51, 52, and 58) are linked to cervical, vulvar, vaginal, and anal cancers, whereas non-oncogenic or low-risk types (6, 11, 43, 44, 40, 42, and 54) are linked to genital warts. Human papillomavirus 16 is the most cancer-causing, accounting for over half of all cervical cancers, while Human papillomavirus 16 and 18 together account for roughly 70% of cervical cancers. The most frequent strains associated with genital warts are Human papillomavirus 6 and 11, which account for over 90% of these lesions. **(Kari P. Braaten and Marc R. Laufer, 2008)**[15]

Figure 2: Types of Human papillomaviruses

Table 1. HPV classification according to the International Agency for Research on Cancer

Classification	HPV types
Group 1. Carcinogenic (high risk)	16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68
Group 2A. Probably carcinogenic (high risk)	68
Group 2B. Possibly carcinogenic (average risk)	26, 53, 66, 67, 70, 73, 82
Group 2B. Risk is unknown	30, (34), 69, (85), 86, (97)
Group 3. Low risk	6, 11, 40, 42, 43, (44), 54, 61, (71), (72), 81, 89, 90

Source: Gusakov K.I et al., 2020[16]

Etiology

There are more than hundred varieties of Human papillomavirus. Some of these cause common warts on the skin. Some infect the anogenital region's skin and mucosa, as well as the oropharyngeal and laryngeal areas.

Important manifestations of anogenital Human papillomavirus include

- Genital warts (condyloma acuminatum)
- Anal, laryngeal, bladder, and oropharyngeal cancers
- Intraepithelial neoplasia and carcinoma of the anus, cervix, or penis
- Bowenoid papulosis

Condylomata acuminata, like laryngeal and oropharyngeal warts, are benign anogenital warts caused by Human papillomavirus strains 6 and 11. Human papillomavirus can induce high - and low-grade intraepithelial neoplasia and cancer. Cervical cancer is caused by Human papillomavirus in almost every case; roughly 70% of cases are caused by types 16 and 18, while the rest are caused by types 33, 31, 35, and 39. Human papillomavirus types that primarily damage the anogenital area can be transmitted to the oropharynx by orogenital contact; type 16 seems to be responsible for a large number of occurrences of oropharyngeal cancer. Human papillomavirus types 16 and 18 can cause cancer in the vulva, vagina, and penis, among other places.

Human papillomavirus is spread from lesions of one person to other through skin-to-skin contact. The types affect the anogenital region are commonly transmitted sexually by penetrative vaginal or anal intercourse, although they can also be spread through digital, oral, or non-penetrative genital contact.

Immunocompromised persons are more likely to develop genital warts. Warts can grow at different speeds but pregnancy, immunosuppression, or skin maceration can speed up their growth and spread. **(Sheldon R. Morris, 2020)**[17]

Risk factors

Risk factors for Human papillomavirus infection include

- First intercourse at an early age
- Engaged in sex with several partners
- Low socioeconomic status
- Engage in unprotected sex or sexual contact
- Persistent Human papillomavirus infection
- Oral contraceptives increasing cervical cancer risk
- Man who has sex with men
- Transgender
- Chlamydia and possibly herpes simplex virus infection
- HIV or other causes of immunodeficiency
- Having more than three full-term pregnancies
- Anal fistula increasing anal cancer risk
- Cigarette smoking **(Elizabeth Boskey and Anita Sadaty, 2021)**[18]

Signs and symptoms

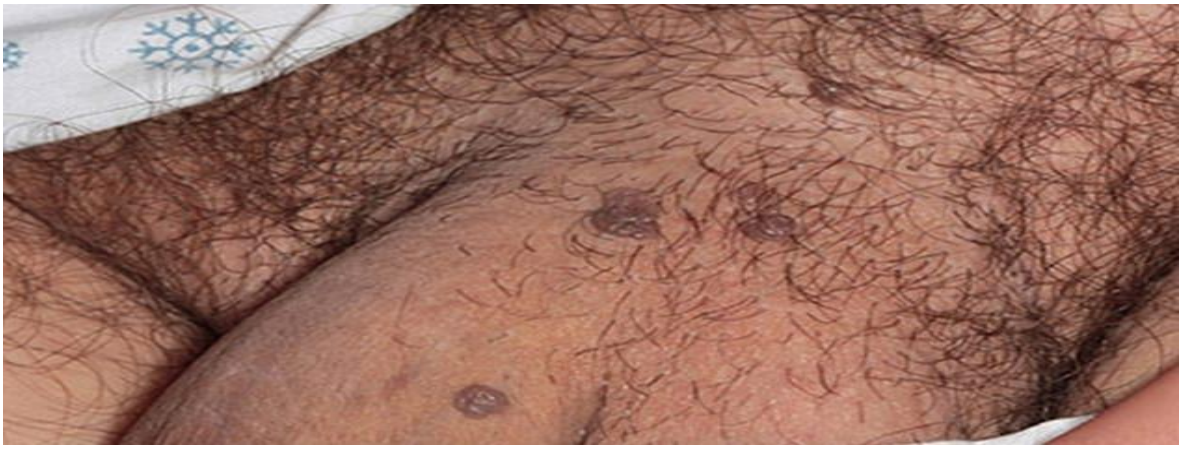
Signs and symptoms of Human papillomavirus infection in men

In men, Human papillomavirus infection usually causes no symptoms, though some Human papillomavirus types can cause genital warts, which show as elevated lumps or bumps on the genital areas. The size of genital warts can range from enormous to little, and they can be flat or elevated. The edges might be smooth or serrated (like a cauliflower).

In men, various kinds of Human papillomavirus infection have been linked to malignancies of the penis or anus. Oropharyngeal malignancies, which affect the throat and involve the base of the tongue and tonsils, are another malignancy that can be caused by Human papillomavirus infection.

Skin warts are another symptom of Human papillomavirus infection, albeit the types of Human papillomavirus that cause skin warts differ from those that cause cancer or vaginal warts.

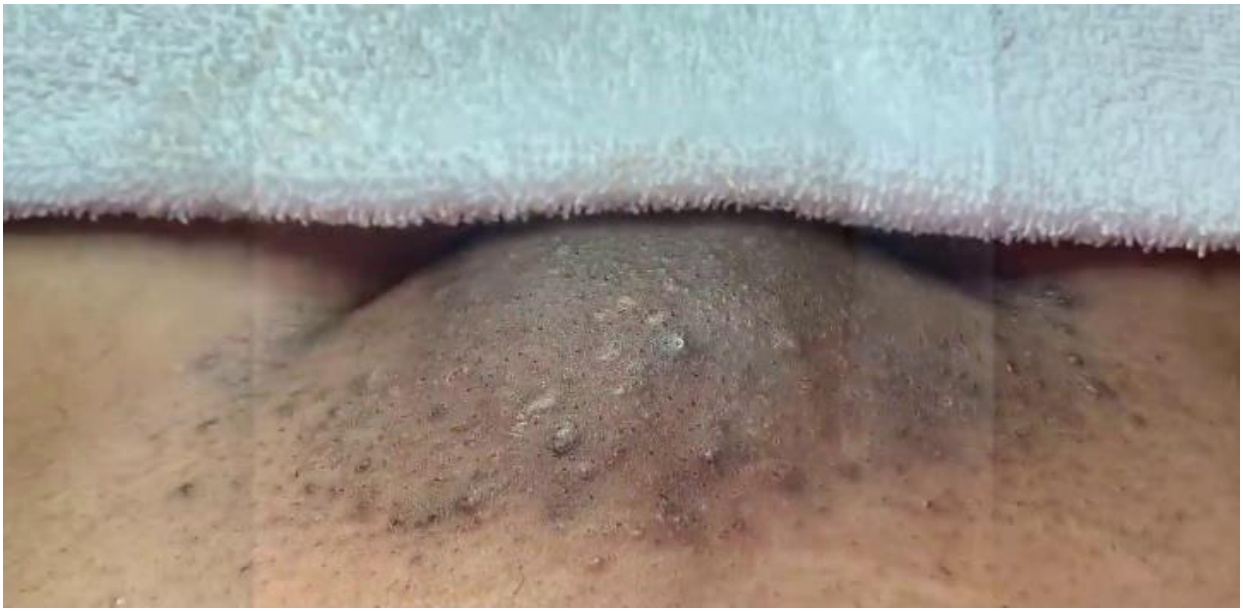
Figure 3: Male genital warts



Source: Mayo Clinic, 2021[19]

Signs and symptoms of Human papillomavirus infection in women

Figure 4: Female genital warts



Source: Geoffrey Nevine, 2021[20]

As with men, Human papillomavirus in women usually does not produce signs or symptoms. However in some cases the Human papillomavirus infection persists and leads to skin warts, genital warts, cancerous and precancerous changes in the cells line the uterine cervix.

Cervical papanicolau (Pap) testing enables for early detection of Human papillomavirus related alterations in the cervix and used as a screening technique for cervical cancer for decades. Human papillomavirus strains that cause cervical cancer and other cancers are known as "high-risk" Human papillomavirus types. **(Melissa Conrad Stoppler and John P. Cunha, 2021)**[21]

Pathophysiology

Human papilloma virus is commonly spread to humans through sexual contact. At every phase, the Human papillomavirus life cycle is connected to epithelial differentiation and maturation of host keratinocytes, as well as transcription of particular gene products. The pathophysiology of cancer-causing HPV infection is primarily tied to high-risk Human papillomavirus types (16, 18, 52, 56, 58, 31, 33, 35, 39, 45, 51, 59, and 68). Human papillomavirus E6 and E7 protein products interact with two critical cell cycle control proteins in the host cell, P53 and Rb, resulting in unrestrained cellular replication and the accumulation of mutations that lead to cancer.

Protein role in the virus life cycle

E1- Genome replication: ATP-dependent DNA helicase.

E2- Genome replication, transcription, segregation, encapsidation; Regulation of cellular gene expression; Cell cycle and apoptosis regulation

E4- Remodels cytokeratin network. Cell cycle arrest, Virion assembly

E5- Control of cell growth and differentiation, Immune modulation

E6- Oncoprotein, Inhibits apoptosis and differentiation; Regulates cell shape, polarity, mobility and signalling

E7- Cell cycle control, Controls centrosome duplication

L1- Major capsid protein

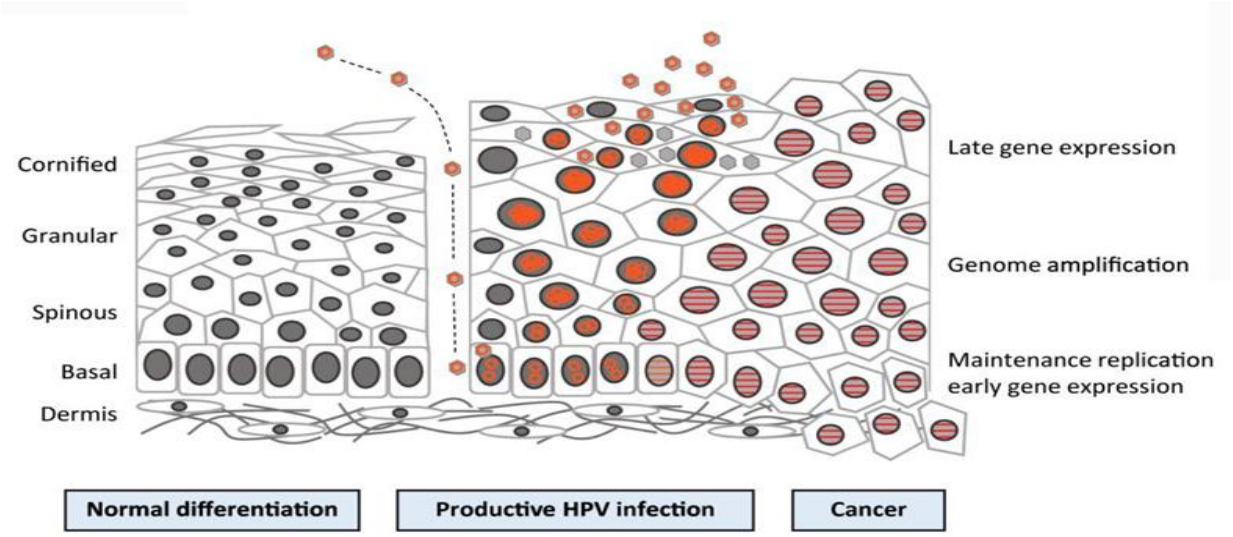
L2- Minor capsid protein; Recruits L1; Virus assembly **(SV Graham, 2012)**[22]

Transmission

- Human papillomavirus is usually transmitted via the sexual route to the human host
- Different types of Human papillomavirus has a predilection for different types of epithelial tissue

HPV life cycle

Figure 5: Human papillomavirus (HPV) life cycle and cancer

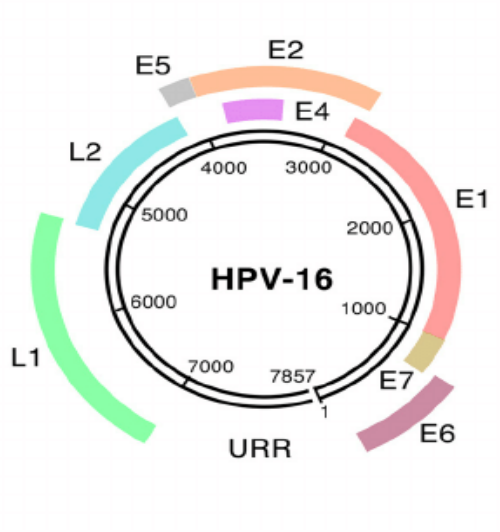


Source: Xuelian Wanget al., 2018[23]

- Human papillomavirus life cycle is linked to epithelial differentiation and maturation of host keratinocytes, with transcription of specific gene products at every level
- Human papillomavirus primarily infects basal cell layer of stratified squamous keratinised epithelium.

- Following transmission, Human papillomavirus uses microabrasions to enter basal stem cell tissue specific heparan sulfate proteoglycans through clathrin mediated endocytosis and caveolin-mediated endocytosis depend on Human papillomavirus
- It undergoes viral uncoating and viral DNA genome is transported to nucleus maintaining a low copy number 10-200 viral genomes per cell
- A sophisticated transcriptional cascade occurs as host keratinocyte begins to divide become increasingly differentiated in upper layers of the epithelium
- Human papillomavirus uses host DNA replicative machinery to multiply it lacks DNA polymerase activity
- Specific viral genes are transcribed at every level of keratinocyte differention
- Early proteins E1, E2, E5, E6, E3, E4, and E7 proteins are synthesized in middle layers, for reactivation of replication process in the differentiated cells
- Late proteins L1, L2 proteins are transcribed in most superficial layers for virion assesmbly, release and reinfection code for capsid proteins **(C. Michael Gibson et al., 2021)**[24]

Figure 6: HPV-16 genome and transforming activity of E6 and E7



Source: Angelika B. Riemer et al., 2010[25]

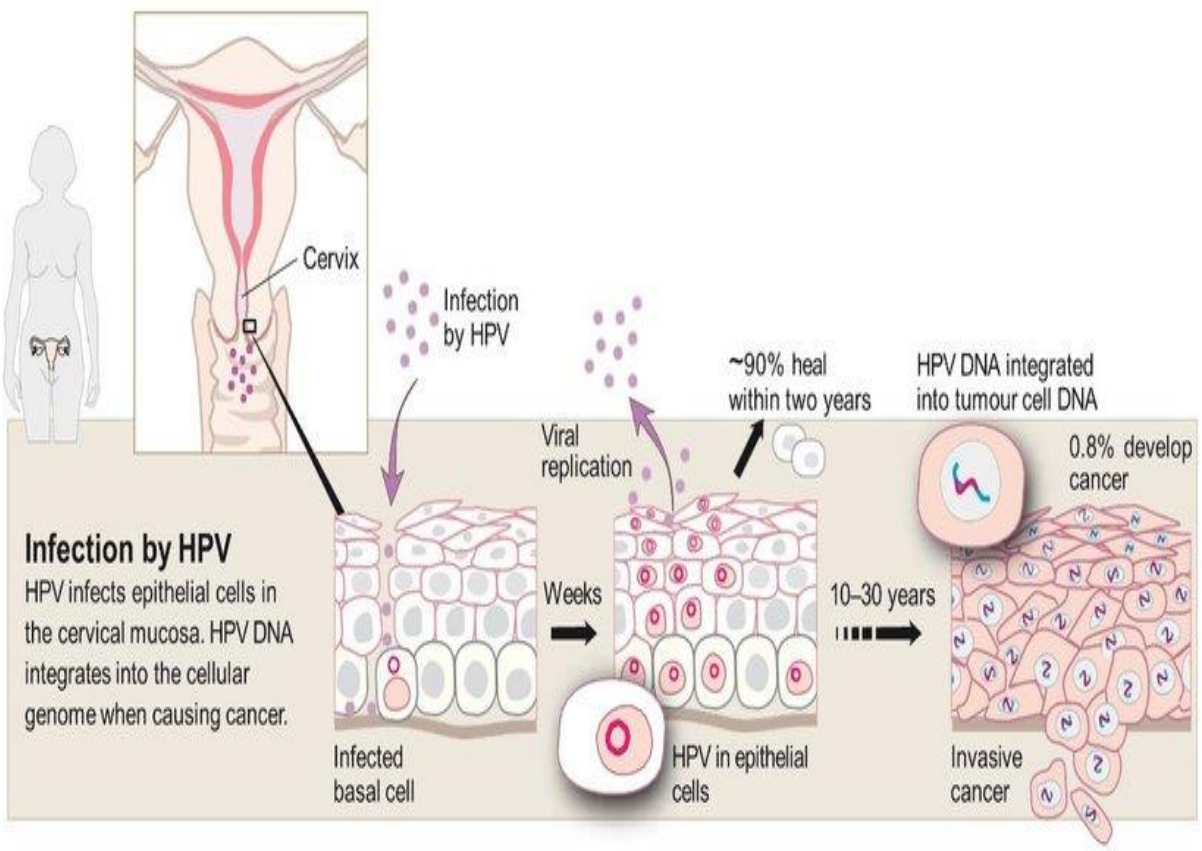
Pathogenesis of HPV infection induced cancers

E6 and E7, two Human papillomavirus proteins, are thought to play a role in the pathogenesis of HPV-related cervical malignancies. From cervical intraepithelial neoplasia grade- 1 to 3 the phenotype of cervical neoplasia was indicated to change depending on the expression levels of E6 and E7 (CIN1 to CIN3). These connections between Human papillomavirus proteins and the host cell's biological pathways may provide prospective targets for Human papillomavirus based cancer treatment techniques. Furthermore, the E2 gene is thought to play a role in cervical cancer since full-length viral genomes are expressed in roughly 35% of Human papillomavirus induced cervical malignancies. When viral DNA fuses with the chromosomes of the cell, the regulation of gene expression is altered. This integration results in the continual expression of E6 and E7 proteins, resulting in the accumulation of cellular DNA alterations and the promotion of cancers. Monosomies, trisomies, structural alterations,

chromatid gaps and breaks, and double minutes, among other mutations, are frequently found in cervical malignancies and other epithelial tumors.

The fundamental mechanism of progression from CIN1 to CIN2, CIN3 and finally cancer is unknown; it could be related to early integration events in CIN1 or viral gene expression dysregulation. It's also plausible that the initial deregulation induces chromosomal instability and integration. The integration is thought to occur in high-grade lesions like CIN2 and CIN3, deregulation of E6 and E7 expression may increase or constant. Flat warts are similar to CIN1 lesions in this scheme, but the cell proliferation level is lower in the basal and parabasal layers. CIN2+ phenotypes are caused by increased E6 and E7 expression levels in high-risk HPV type infections. This trait causes genetic alterations that aid in the growth of cancer. These findings imply that decreased E6 and E7 expression has no effect on the function of CIN1's cellular targets and thus does not contribute to cancer progression. The viral episome is helped into the host cell chromosome by viral dysregulation in CIN2/ CIN3+. Deregulation of E6 and E7 expression may result as a result of this. Young women have CIN2+ soon after infection according to clinical vaccine trials. It's probable that deregulation of gene expression is caused by cell signaling changes or epigenetic modifications, such as viral DNA methylation, in these circumstances. **(Pinar Tulay and Nedime Serakinci 2016)**[26]

Figure 7: Pathogenesis of HPV in cervical cancer



Source: Holger Stark and Aleksandra zivkovic, 2018[27]

HPV-Induced Diseases

- Common warts are associated with Human papillomavirus types 2, 4 (most common), followed by types 1, 27, 29, 3, and 57
- Flat warts are caused by types 10, 3, and 28
- Deep palmoplantar warts are caused by types 1 (most common) followed by types 4, 27, 2, 3, and 57

- Cystic warts are caused by type 60
- Focal epithelial hyperplasia is caused by types 13 and 32
- Butcher's warts are caused by type 7 **(Ahmad M. Al Aboud and Pramod K. Nigam, 2021)**[28]

Diagnosis

Traditional viral diagnosis approaches such as cell culture, electron microscopy and certain immunological procedures, are ineffective in detecting Human papillomavirus. The human papillomavirus cannot be cultivated in cell cultures.

The important methods to diagnose Human papillomavirus infection are

- ❖ Pap smear
- ❖ Colposcopy and acetic acid test
- ❖ DNA test (Southern Blot Hybridization, PCR, In Situ Hybridization)
- ❖ Biopsy

PAP smear or PAP test

Papanicolaou and Traut were the first to characterize it as a screening test.

Virus infections such as Human papillomavirus infection and Herpes can also be discovered, in addition to premalignant and malignant alterations.

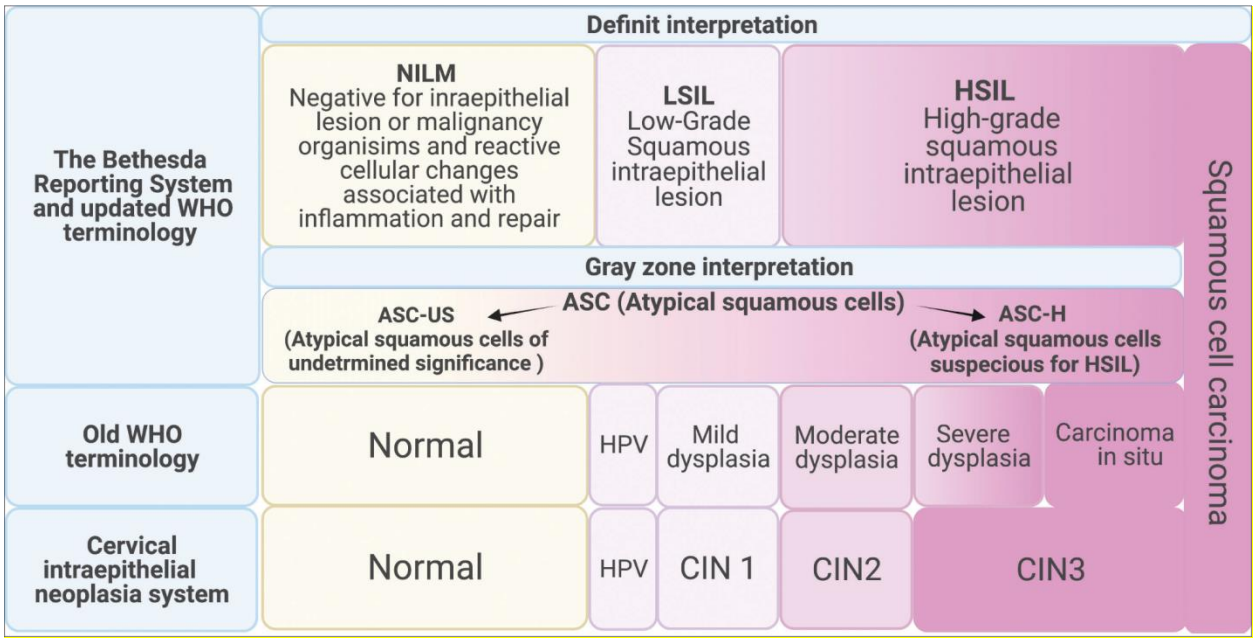
A positive test necessitates additional confirmation tests such as a cervical biopsy, a coloscopy, and DNA tests such as PCR.

Procedure

The patient is positioned in the dorsal position, and the cervix is exposed with Cusco's speculum, which is used to scrape the squamocolumnar junction with Ayre's spatula by spinning it all around.

The scrapings are applied on a glass slide that has been fixed with 95 percent ethyl alcohol and ether, or a fixative spray (cytospray).

Scrapings are collected from the top lateral section of the vaginal wall for cytological examination.



ACOG revised recommendations for Pap smears are

Women between the ages of 21 and 30 should be screened every two years rather than once a year, using either the normal Pap test or liquid-based cytology.

Women over age of 30 have had three consecutive negative cervical cytology test results may be screened with either the Pap or liquid-based cytology once every three years or can be extended to five years if HPV is cotested.

Women who have HIV are immunosuppressed, have been exposed to diethylstilbestrol in utero, have treated for cervical intraepithelial neoplasia CIN 2 and CIN 3 cervical cancer may require more regular screening. **(Rahul Dixit et al., 2011)[31]**

Colposcopy and acetic acid test

Colposcopy is an outpatient technique performed by specially educated clinicians using a low-powered microscope called a colposcope.

Colposcopy is the examination of the vagina, cervix and in some cases, the vulva following administration of an acetic acid solution, as well as the collection of colposcopically directed biopsies of all lesions suspected of neoplasia.

The degree of acetowhite lesion, surface contour, mosaic pattern and punctuation are all considered when grading colposcopic findings. The severity of lesions is related to severity of these characteristics.

Acetic acid test

- Soaking acetic acid into suspicious lesions enhance degree of suspicion in lesions without classic features
- The method involves applying a 3–5% acetic acid moistened gauze pad for 5-10 minutes on suspected lesions of cervix, labia, penis or perianal area
- Inconspicuous, genital lesions, flat, that might be difficult to assess become visible. Dysplastic, Genital warts and neoplastic tissues turn white
- False-positive results are common and can result from anything that causes parakeratosis like candidiasis, healing epithelium, psoriasis, lichen planus, sebaceous glands
- The acetic acid test should not used for routine screening
- It used for visualizing subclinical genital Human papillomavirus associated lesions, identifying lesions for target biopsy and for demarcating lesions during surgical therapy **(Carolyn K Martin et al., 2011)**[29]

The use of colposcopy screening is only to be recommended for

- ❖ Immunosuppressed transplant recipients
- ❖ Human immunodeficiency virus positive women
- ❖ Women with three consecutive inadequate samples will be referred for colposcopy after three tests in a series show borderline nuclear change in squamous cells, and women with one test report borderline nuclear change in endocervical cells will be referred for colposcopy

- Cervical cytology reveals cancerous or worrisome cells, although the cervix appears clinically normal
- After 2 tests reveal mild dyskaryosis, women must be referred.
- After 1 test results in moderate or severe dyskaryosis, women must be referred for colposcopy. At least 90 percentage of women with such test findings should be seen in a colposcopy clinic within 4 weeks after referral. After 1 test that indicates potential invasion or glandular neoplasia, women must be referred for colposcopy and 90 percent of them should be examined immediately within 2 weeks of referral.

Biopsy

Colposcopy enables for targeted tissue sampling (biopsy) of aberrant locations. The biopsy of abnormal areas is an important element of colposcopy since the severity of the abnormality on the biopsy sample will determine the treatment. Treatment is recommended if the biopsy results reveal pre-cancer (dysplasia) or malignancy. Mild, moderate or severe dysplasia can occur.

When colposcopic appearances indicate a high-grade abnormality, when low-grade colposcopic alteration is coupled with severe dyskaryosis or worse or when a lesion spreads into the canal, excisional biopsy is recommended.

The presence of koilocytes, mature squamous cells with a distinct perinuclear zone, is the most distinguishing feature of genital warts. Koilocyte nuclei can be larger and hyperchromatic and double nuclei are frequently encountered.

DNA techniques

Direct probe hybridization methods such as dot blot and Southern blot were initially employed to detect Human papillomavirus. They had low sensitivity, required huge amounts of DNA in clinical samples, and have mainly been replaced by amplification technology, which has permitted detection of low-level virus copy numbers in clinical samples. Hybridization of viral nucleic acids is a well-established regular approach for viral detection.

The 2 main techniques are

1. Hybrid capture Human papillomavirus DNA Test

Hybrid capture Human papillomavirus DNA Test in conjunction with the Pap test is now approved by FDA. **(Jeanne S Mandelblatt et al., 2002)[30]**

The FDA-approved Hybrid Capture two tests may identify as low as 1 pg of Human papillomavirus DNA/ml, making its sensitivity and specificity approximately identical to PCR-based detection methods. The advantages of Hybrid Capture two test include its ease of use and high reproducibility of results, making it the best standardized Human papillomavirus detection tool available. While the exact Human papillomavirus type cannot be determined, "low-risk" (6, 11, 42, 43, and 44) and "high-risk" (16, 18, 31, 52, 56, 58, 59, 33, 35, 39, 45, 51, and 68) Human papillomavirus genotype groups (HR HPV and LR HPV) HPV genotype groups (HR HPV and LR HPV) Human papillomavirus genotype groups (HR HPV and LR HPV) Human papillomavirus genotype groups (HR HPV) are detected.

2. Polymerase chain reaction

PCR is a selective target amplification technology that can exponentially and repeatedly increase the quantity of Human papillomavirus sequences in biological specimens. A single double-stranded DNA molecule can theoretically create one billion copies after 30 cycles of amplification.

Indications

In conjunction with the Papanicolaou test, primary screening is performed.

Test for women over 30 years of age or as a Stand-Alone Test in women over 30 years

Potential Complications of Human papillomavirus Infection

- Cervical cancer
- Vulvar cancer
- Vaginal cancer
- Penile cancer
- Anal cancer
- Cancer of the back of the throat **(Joseph Bennington-Castro and Sanjai Sinha, 2018)**[32]

Abnormal cervical cytology

An abnormal cervical screening test result is changes in the cells covering the cervical os. These changes may not be cancer. The cells often back to normal by themselves. **(Cancer Research UK, 2020)**[33]

Risk-Based Management Consensus Guidelines for Abnormal Cervical Cancer Screening Tests and Cancer Precursors

- Recommendations are based on risk

    - Recommendations of colposcopy, treatment, or surveillance will be based on a patient's risk of CIN 3+ determined by a combination of current results and past history. The same current test results may yield different management recommendations depending on the history of recent past test results.

- Colposcopy can defer for certain patients.

    - Repeat human papillomavirus testing or co testing at 1 year is recommended for patients with minor screening abnormalities indicating Human papillomavirus infection with low risk of underlying CIN 3+ (eg HPV positive, low-grade cytologic abnormalities after a documented negative screening Human papillomavirus test or co test).

- Guidance for expedited treatment is expanded (treatment without colposcopic biopsy).

    - Expedited treatment was an option for patients with high-grade squamous intraepithelial lesion (HSIL) cytology in the 2012 guidelines; this guidance is now better defined.

    - For nonpregnant patients 25 years or older, expedited treatment, defined as treatment without preceding colposcopic biopsy demonstrating CIN 2+, is

preferred when the immediate risk of CIN 3+ is ≥ 60%, and is acceptable for those with risks between 25% and 60%. Expedited treatment is preferred for nonpregnant patients 25 years or older with HSIL cytology and concurrent positive testing for HPV genotype 16 (HPV 16) (ie, HPV 16-positive HSIL cytology) and never or rarely screened patients with HPV-positive HSIL cytology regardless of HPV genotype.

- Shared decision making should be used when considering expedited treatment, especially for patients with concerns about the potential impact of treatment on pregnancy outcomes.

❖ Excisional treatment is preferred to ablative treatment for histologic HSIL CIN 2 or CIN 3 in the United States. Excision is recommended for adenocarcinoma in situ AIS.

❖ Observation is preferred to treatment for CIN 1.

❖ Histopathology reports based on Lower Anogenital Squamous Terminology (LAST)/World Health Organization recommendations for reporting histologic HSIL should include CIN 2 or CIN 3 qualifiers, HSIL - CIN 2 and CIN 3.

❖ All positive primary HPV screening tests, regardless of genotype, should have additional reflex triage testing performed from the same laboratory specimen reflex cytology.

- Additional testing from the same laboratory specimen is recommended because the findings may inform colposcopy practice. Human papillomavirus 16 positive HSIL cytology qualifies for expedited treatment.

- Human papillomavirus 18 or 16 infections have the highest risk for CIN 3 and occult cancer, so additional evaluation is necessary even when cytology results are negative.

- Human papillomavirus 18 or 16 testing is positive and additional laboratory testing of the same sample is not feasible the patient proceed directly to colposcopy.

❖ After treatment and initial post treatment therapy of histologic CIN 3, CIN 2, or ASCUS, continued monitoring with Human papillomavirus testing or cotesting at 3-year intervals for at least 25 years is advised. Surveillance at 3-year intervals after 25 years is acceptable as long as the patient's life expectancy and ability to be screened are not jeopardized by substantial health problems.

    - The 2012 guidelines recommended return to 5-year screening intervals and not specify when screening should cease. New evidence indicates risk remains elevated for at least 25 years with no evidence that treated patients ever return to risk levels compatible with 5-year intervals.

❖ Only if testing with Human papillomavirus or cotesting is not possible is cytology alone adequate for surveillance. For the detection of precancer, cytology is less sensitive than Human papillomavirus testing, hence it is advised more frequently. When Human papillomavirus testing or cotesting is advised annually cytology is recommended every

six months. When Human papillomavirus or cotesting is advised at 3-year intervals, cytology is recommended once a year.

- Human papilloma virus assays that are Food and Drug Administration approved for screening should be used for management according to their regulatory approval in the United States.

    - For all management indications, Human papillomavirus mRNA and Human papillomavirus DNA tests without FDA approval for primary screening alone should only are used cotest with cytology unless sufficient rigorous data are available to support use of these particular tests in management. **(ACOG, 2020)**[34]

Summary of Cervical Cancer Screening Recommendations:

Age	ACS (2020)	ACOG (2016, 2018)	USPSTF & AAFP (2018)
<21 years	Not recommended	Not recommended	Not recommended
21-29	***Start at 25 years*** Primary HPV testing alone every 5 years (preferred) **OR** Co-testing every 5 years **OR** Cytology alone every 3 years	***Start at 21 years*** Cytology alone every 3 years	***Start at 21 years*** Cytology alone every 3 years
30-65	Primary HPV testing alone every 5 years (preferred) **OR** Co-testing every 5 years **OR** Cytology alone every 3 years	Co-testing every 5 years (preferred) **OR** Cytology alone every 3 years **OR** Primary HPV testing alone every 5 years [b] (alternative)	Cytology alone every 3 years **OR** Primary HPV testing alone every 5 years **OR** Co-testing every 5 years (alternative)
>65	Not recommended [a]	Not recommended [c]	Not recommended [c]
Hysterectomy (with no history of cervical cancer or high-grade pre-cancerous lesion)	Not recommended	Not recommended	Not recommended

[a] No CIN 2 or greater within 25 years ***and*** documented negative screening in prior 10 years

[b] Acceptable in women ≥ 25 years

[c] History of adequate screening: 3 consecutive negative cytology results or 2 consecutive negative co-testing results within 10 years with the most recent test within 5 years

Prevention of HPV

Primary prevention	Secondary prevention	Tertiary prevention
• Girls 9-14 years • Human papillomavirus vaccination	• Women 30 years old or older	• All women as needed
• Girls and boys, as appropriate • Health information and warnings about tobacco use • Sex education tailored to age and culture • Male circumcision • Promotion and distribution of condoms to people who engage in sexual activity	• Screening with a high-performance test that is comparable to or better than the Human Papillomavirus test. • Pre-cancer lesions should be treated immediately or as soon as feasible.	• Treatment of invasive cancer at any age • Surgery • Chemotherapy • Palliative care • Radiotherapy

HPV vaccination

There are presently three prequalified vaccines available, all of which protect against both Human papillomavirus 18 and 16 which are known to cause at least 70% of cervical malignancies. The third vaccine protects against five more oncogenic Human papillomavirus varieties, which are responsible for another 20% of cervical malignancies. WHO considers three vaccines equally protective against cervical cancer because the vaccines that solely protect against Human papillomavirus 18 and 16 also have some cross-protection against these other less frequent HPV strains that cause cervical cancer. Human papillomavirus types 11 and 6, which produce anogenital warts, are also protected by two of the vaccines.

HPV vaccinations have been found to be very safe and successful in preventing Human papillomavirus infections, high-grade precancerous lesions, and invasive malignancy in clinical trials and post-marketing surveillance.

When given before being exposed to HPV, Human papillomavirus vaccinations work best. World Health Organization recommends immunizing females between the ages of 9 and 14, when the majority of them have not started sexual conduct. Human papillomavirus infection or Human papillomavirus related illnesses like cancer are not treatable but only preventable with vaccinations. Some countries have begun to vaccinate boys because the vaccine prevents genital malignancies in both males and females and two current vaccines also protect males and females from genital warts.

The immunization of girls aged 9 to 14 years is recommended by the WHO as the best cost-effective public health strategy against cervical cancer.

Cervical cancer screening is not replaced by Human papillomavirus vaccination. Screening programs may need to be developed or strengthened in countries where the Human papillomavirus vaccine has been introduced.

Screening and treatment of pre-cancer lesions

Cervical cancer screening includes tests for pre-cancer and malignancy, as well as an increasing number of tests for Human papillomavirus infection. Even women who have no symptoms and appear to be in good condition are to be tested. When Human papillomavirus infection or pre-cancerous lesions are detected during screening, they can be readily treated, and cancer can be averted. Cancer can also be detected early with screening, and treatment has a good cure rate.

Because pre-cancerous lesions take a long time to grow, all women should be screened beginning at the age of 30 and on a regular basis after that (frequency depends on the screening test used). Women who are sexually active and have Human papillomavirus should be tested as soon as they find out their status.

Positive screening test results must be treated and managed in tandem with the screening process. Conducting screenings without adequate management in place is unethical.

There are three different types of screening tests that are currently recommended by World Health Organization

- **HPV DNA testing for high-risk HPV types**
- **conventional (Pap) test and liquid-based cytology (LBC)**
- **Visual inspection with Acetic Acid (VIA)**

Cryotherapy or thermal ablation, as well as Loop Electrosurgical Excision Procedure (LEEP) when available, are recommended by World Health Organization for the treatment of pre-cancer lesions. Women with advanced lesions should be referred for additional testing and treatment.

Management of invasive cervical cancer

When a woman has symptoms that suggest she may have cervical cancer, she should be referred to a specialist for additional diagnosis, evaluation and treatment.

Symptoms of early stage cervical cancer include

- Irregular blood spotting or light bleeding between periods in women reproductive age
- Bleeding after sexual intercourse
- Postmenopausal spotting or bleeding
- Increased vaginal discharge, sometimes foul smelling

As cervical cancer advances, severe symptoms may appear including

- loss of appetite , Weight loss, fatigue
- leg and/or pelvic pain , Persistent back
- vaginal discomfort and Foul-smell discharge
- Swelling of leg lower extremities

Other severe symptoms arise at advanced stages depending on which organs cancer spread.

Histopathologic testing is required to diagnose cervical cancer. The stage is determined by the size of the tumor and the extent to which the cancer has spread throughout the pelvis and to distant organs. Depending on the stage of the disease, surgery, radiation, and chemotherapy are all options. Palliative care is an important element of cancer treatment that helps patients cope with the pain and suffering that comes with the disease. **(WHO, 2020)**[35]

HISTORY

Harald zur Hausen awarded Nobel Prize in Physiology or Medicine in 2008 for discovering link between Human papillomavirus and cervical cancer in the 1980s. Over the next decade, more research will be conducted to confirm the link between certain Human papillomavirus genotypes and cervical cancer. So far, 14 high-risk Human papillomavirus genotypes have been linked to cancer, with Human papillomavirus 16 and 18 accounting for 70% of cervical malignancies and pre-cancerous lesions. Thankfully, infection does not always lead to cancer. Despite the fact that some women are infected with these high-risk viruses, they show no symptoms. Their immune system may even be able to completely eliminate the illness. Others, on the other hand, are dealing with medical issues as a result of their illness. **(Kayla M. Hager, 2019)**[36]

Natural History

The human papillomavirus is a tiny DNA virus with a genome of about 8000 base pairs. HPV attacks the basal cells in the stratified squamous epithelium as well as the metaplastic cells in the cervix's squamocolumnar junction. Human papillomavirus can also infect the endocervical glandular epithelium, causing glandular neoplasms as adenocarcinoma in situ or invasive adenocarcinoma. E6 and E7 are the two main oncogenes found in high risk Human

papillomavirus strains. These 2 genes are expressed early in the Human papillomavirus life cycle, as indicated by the "E" designation. The products of these two genes change the metabolism of the host cell, promoting neoplastic growth. E6 attaches to and destroys the p53 protein in the host cell. This targeted degradation has the effect of preventing apoptosis in infected host epithelial cells. Telomerase is also active, enhancing oncogenic alterations even further. By attaching to retinoblastoma protein and blocking its function the E7 protein has a comparable effect on cell metabolism. The cell cycle is disrupted as a result of this. E6 and E7 proteins can also destabilize chromosomes by inhibiting cyclin-dependent kinase inhibitors and host interferons.

Human papillomavirus E7 and E6 expression levels are highly correlated with the type of cervical lesion E7 and E6 are expressed at low levels in the basal cells and higher levels in the upper layers of the epithelium in low-grade lesions, whereas E7 and E6 are expressed at high levels throughout the epithelium in high-grade lesions. Human papillomavirus DNA is episomal in low-grade lesions, but it is more likely to have been integrated into the host-cell chromosome in higher-grade lesions and cancer. The integration of Human papillomavirus DNA into host DNA promotes cellular proliferation and increases the risk of cancer.

Unlike many other genitourinary infections, Human papillomavirus infection does not usually cause acute symptoms like burning, itching, or vaginal discharge. Rather, because most infections are resolved by the host immune system, the majority of persons infected with HPV will not acquire clinical disease or symptoms. Only 24.8 percent of women infected with HPV 6 or 11 got genital warts in one study. For the period of a large, prospective 10-year cohort study of more than 20,000 women enrolled in a health maintenance organization, the incidence of CIN 3 or cancer was around 7% among HPV-positive women. Only a small percentage of people with

Human papillomavirus infections experience major clinical consequences. The specific process by which the host immune system clears Human papillomavirus infection is unknown at this time.

An increased incidence of initial infection and/or clinical sequelae such as genital warts, CIN, or invasive malignancy has been linked to a number of variables. Smokers are more likely to get cancer, and it is believed that smoking raises the risk of developing SIL. Cervical cancer is also linked to infection with the herpes simplex virus (HSV) and C. trachomatis. In a pooled research, Smith et al discovered that earlier exposure to HSV-2 was linked to a 2-fold greater risk of cervix squamous cell carcinoma in patients with Human papillomavirus; C. trachomatis infection is linked to a similar increased risk of squamous cell carcinoma. Infection with C. trachomatis is also linked to more persistent HPV infection, which could raise the risk of clinical consequences from HPV infection in those who are also infected with C. trachomatis.

Human papillomavirus infection and HPV-related illness are particularly dangerous for immunocompromised and HIV-positive people. High HIV RNA levels and CD4 counts below 200 cells per mm3 are linked to both incident and persistent Human papillomavirus infection, though the link between incident and persistent infection is stronger. HIV-positive women with low CD4 cell counts are more likely to acquire SIL than HIV-positive women or negative women with high CD4 cell counts in women with oncogenic Human papillomavirus. **(Kevin A. Ault, 2006)**[37]

Available Vaccines and Vaccination Campaigns history

Gardasil (HPV4), a Merck vaccine for four forms of Human papillomavirus, was authorized by the US Food and Drug Administration in 2006. In 2009, the FDA authorized

GlaxoSmithKline's Cervarix (HPV2) vaccination, which protects against two high-risk strains of HPV. In 2014, a nine-valent vaccine (HPV9, Gardasil 9) received FDA approval. All Human papillomavirus vaccinations contain only a protein derived from the shell of certain Human papillomavirus types; they do not contain viral RNA or DNA and so cannot cause disease. Precancerous cervical alterations and precancerous anal changes in women and men caused by high-risk cancer-causing Human papillomavirus strains have been demonstrated to be prevented by Human papillomavirus vaccinations. HPV4 and HPV9 also protect against a number of low-risk Human papillomavirus strains that cause warts.

Advisory Committee on Immunization Practices' current recommendations and guidelines for Human papillomavirus vaccination for females and males are listed below

- Female between ages of 11 and 12 should be vaccinated against Human papillomavirus. Children as young as nine years old can receive the vaccine series. Female between ages of 13 and 26 have never been vaccinated should get vaccinated.
- Males aged 11 to 12 years old should be vaccinated against HPV4 or HPV9 on a regular basis. Starting the vaccine series as early as 9 years old is possible. Males aged 13 to 21 who have not been vaccinated previously or who have not completed the series should get HPV4 or HPV9 vaccines. Immunization is available to males between the ages of 22 and 26.
- If the vaccination series is started before the age of 15, all adolescents will receive a 2 dose series. Three vaccination doses are given if the series is started at the age of 15. **(History of Vaccines, 2020)**[38]

EPIDEMIOLOGY

In India

Cervical cancer has been the most common cancer in women over the past 2 decades. Cervical cancer is most common between the ages of 55 and 59 in India. According to the National Cancer Registry Program, the most prevalent cancer sites in women are the breasts and cervix. According to NCRP data, between 2009 and 2011, the Aizawl district in India's north-east had the highest age-adjusted cervical cancer rate of 24.3, followed by Barshi Expanded at 19.5, and Bangalore at 18.9. The age-adjusted rate in the Bangalore registry declined from 32.4 in 1982 to 18.7 in 2009, from 22.1 in 1988 to 14.1 in 2010, from 41 to 16.7 in 2009 in Chennai, and from 9.2 in 2005 to 7.7 in 2011. In the years 1982 to 2010, the annual percentage drop ranged from 1.3 percent in Bhopal to 3.5 percent in Chennai.

Since 1995, the Bangalore Cancer Registry has shown a downward trend. Because the cause of death is frequently unknown, the NCRP's cervical cancer mortality figures are insufficient. During a 30-year study period in the Mumbai registry, there was an estimated yearly percent change in cervical cancer of 1.8 percent (95 percent CI: 2.0, 1.6), which was linked to a significant increase in breast cancer. Cervical cancer rates declined by 1.8 percent each year on average among women aged 30 to 64, but they still accounted for 16 percent of all female cancers. However, between 1983 and 1987 and 2003 and 2007, the percentage of all cervical cancers fell from 43.8 percent to 37.6 percent. In Odisha, on the other hand, cancer of the cervix was the second most prevalent malignancy, with a 3.1 percent increase from 2001 to 2011. The north eastern areas of Tamil Nadu, in the southern part of India, display a different pattern with a high prevalence of cervical cancer and penile cancer. This could be due to infection with the

human papillomavirus, which has also been linked to the development of penile cancer. The human immunodeficiency virus is also prevalent in this area. Cervical cancer is very common in South and Southeast Asian countries, owing to a high incidence of HPV (more than 10% in women over 30 years old) and a lack of screening.

HPV-16 and 45 were shown to be much more common in North India, while HPV-35 was found to be significantly more common in South India. Persistence was found to be higher for high risk Human papillomavirus types in a prospective research in Delhi, with the highest rates of persistence identified in types 16, 31, 51, 45, 67, 59. The average duration of HPV-16 persistence among high-risk types was 12.5 months. In a Delhi slum, the Human papillomavirus infection rate was found to be 5 per 1,000 woman-months among healthy women. In young, HPV-negative women, the cumulative incidence of a first Human papillomavirus infection has been estimated to be 32 percent at 24 months and 43 percent at 36 months. **(Palika Datta et al., 2012)**[39]

High risk Human papillomavirus was linked to rising age, low education, physical labor, early age at first sexual intercourse, and widowhood/separation in Maharashtra. In eastern India, the risk of Human papillomavirus infection was shown to be higher in married women and women with a parity of >4.37. Human papillomavirus infection was found to decrease dramatically with age, but other infections rose with age. Human papillomavirus infection reduced dramatically as the age of cohabitation increased. HPV infection is widespread in Indian women between the ages of 26 and 35, a decade later than in Western nations, and cancer occurs between the ages of 45 and 59. There is a considerable time between infection and aggressive malignancy, providing ample opportunity for prevention. **(Aswathy Sreedevi et al., 2015)**[40]

In Worldwide

Human papillomavirus infection has reached a significant proportion of the global population, especially among women, where it is the leading cause of cancer, making Human papillomavirus a contemporary public health concern. Human papillomavirus infection has remained one of the most frequent viral illnesses in the world, with an estimated 291 million Human papillomavirus -positive women globally in 2007.

Previous studies found 10.4 percent (11) and 11.7 percent Human papillomavirus prevalence in women with normal cervical cytology (NCC) in 2007 and 2010, respectively, corrected to 9.9 percent in 2019. (7). Oceania (21.8 percent, expected to be 30.9 percent in 2019) and Africa (21.1 percent) had the highest Human papillomavirus prevalence in these women, followed by Europe (14.2 percent), America (11.5 percent), and Asia (11.5 percent) (9.4 percent). In 2011, 32.1 percent of 576,281 gynecologically healthy and unwell women in the overall female population were HPV carriers, with Asia and Africa having the highest prevalence rates of 45.5 and 29.6 percent, respectively.

The Human papillomavirus distribution profile in women with NCC is nearly identical to that of the general female population in terms of geographical globe areas. In poorer countries, it is higher. HPV prevalence was greater in Sub-Saharan Africa (SSA) (24.0%), particularly in Eastern Africa (33.6%) and Latin America, according to the combined research from cytologically healthy women. The highest prevalence of Human papillomavirus in all females was found in Asian regions, where nearly half of Central, Eastern, and Southern Asians (57.7% and 44.4 percent, respectively) were carriers, while in SSA region 42.2 and 32.3 percent of women in Southern and Eastern Africa were carriers, respectively. Human papillomavirus

prevalence was modest (30%) in practically all European countries, including Western Europe (3.7 percent). As a result, Human papillomavirus infection rates in poor countries are greater (42.2%) than in industrialized countries (22.6 percent). Regardless of development, the incidence is high in Eastern Europe (21.4 percent) and low in North Africa (9.2 percent) and Western Asia (2.2 percent). Furthermore, comparable age trends were identified in all of these studies involving females. Adolescent girls and women under the age of 25 were the most affected, while there was a comeback in Human papillomavirus infection among adults over 45 in the African (East and West Africa) and American (Central and Southern America) regions. **(Laia Bruni et al., 2010)**[41]

The global prevalence rate of genital Human papillomavirus infection in men (3.5–45 percent vs. 2–44 percent) is approximately identical to that in women. This is understandable given that anogenital Human papillomavirus is primarily transmitted through sexual contact. Indeed, 9.0 percent of 4,065 healthy men from Africa, America, Asia, and Europe were found to be HPV carriers in a 2014 study. Homosexuals and Human papillomavirus positive males are at higher risk of HPV anal infection (90 percent), compared to heterosexual men, whose risk of Human papillomavirus infection is determined by the number of sexual partners. Furthermore, for all men, the Human papillomavirus infection rate is the same among the young and old, and it varies very little with age. This pattern is distinct from what has previously been observed in women. In terms of regional distribution, the rate of Human papillomavirus infection in men is higher in Africa, particularly among South African men (17.2 percent per year), and lower in Asia (3.2 percent per year). The study indicated that low- and middle-income nations have a greater frequency of all Human papillomavirus genotypes than developed ones.

Taken together, these findings suggest that the highest levels of Human papillomavirus incidence and prevalence are seen in low- and middle-income countries, in both healthy and ill people. In fact, it is well-known that poverty, which is often connected with inactivity, is the leading source of sexually transmitted illnesses, such as Human papillomavirus. Furthermore, the very high prevalence rates of high risk oncogenic genital HPVs (HR-HPVs) reported in young women, especially in low and middle-income countries, can be explained by the fact that most women begin sexual intercourse early. Interestingly, patterns of cultural diversity, such as early marriages followed by high divorce rates, are key variables in enhancing viral transmission in some undeveloped regions, such as SSA and East and Southwest Asia. Furthermore, in SSA, access to screening and healthcare remains a battleground, a difficulty when compared to affluent nations, particularly for women who marry young (10–14 years old), resulting in a lack of health empowerment. **(Marcos Delprato, 2017)**[42]

Because of their strong immunity as well as their sexual and financial stability, some women are able to clear the virus quickly, which explains why Human papillomavirus prevalence declines after the age of 25. The multi-sexual partnership is typically caused by social and financial instability (poor) and a lack of knowledge in older women, resulting in low rates of recrudescence, persistence, or reinfection. **(Jan Henk Dubbink et al., 2016)**[43]

Second, in just three years (from 2007 to 2010), the total prevalence of HPV infection in women with NCC increased by nearly 1% (10.4–11.7%, respectively), following the same trend as the subcontinents previously indicated. According to these findings, if no current vaccination program is introduced or improved by 2025, a rise of roughly 5% in cases of healthy Human papillomavirus positive women could be seen worldwide (17%), mainly in low and middle-income nations. Because of the dynamics of transmission, even though the burden is smaller in

men, the growing rate will be the same. It's worth noting that just because men have a lower Human papillomavirus load than women don’t mean they're poor carriers of the virus. However, given the large number of samples collected from 18 countries (>24,000 participants) and the study's relatively long observation period (1950–2015), it is reasonable to conclude that men have a low clearance rate they are less likely to develop natural anti- Human papillomavirus immunity than women, who clear the infection in a shorter time than men.

The high prevalence of Human papillomavirus in men, which is age-independent, could be explained by their sexual activity with highly infected young girls under the age of 25, as well as the fact that men, compared to women, have a lower potential for developing natural or acquired immunity, even after multiple exposures. This shows that men serve as reservoirs or vector-based niches for Human papillomavirus (particularly HR-HPVs) in women and MSM, while any sexual component serves as a potential transmission mechanism in MSM. We can deduce from this remark that the 1% increase in infection rates found in women may be equivalent in men. **(Arnaud John Kombe Kombe et al., 2021)**[44]

REVIEWS

S. Prathima et al., [45], in his cross-sectional research showed that Cervical cytology was abnormal in 30% of Human papillomavirus positive women, with ten percent having HSIL, fifteen percent having LSIL, and five percent having ASCUS. Significant risk factors related with abnormal Pap smear included age at first sexual intercourse 17 years (p = 0.009), previous H/O STI (p = 0.0001), women with husbands having many sexual partners (p = 0.0001), and women with CD4 count 350 cells/microliter (p = 0.0001). Because of its extended preinvasive stage, invasive cervical cancer is considered a preventable disease. As a result, screening for premalignant cervical lesions offers a chance for women to avoid acquiring cervical carcinoma.

Jiayao Lei et al., [46] in 2020, researchers looked at 153,250 girls born between 1989 and 1993 who had lived in Sweden from the introduction of HPV vaccines. The Swedish National Cervical Screening Registry was used to assess their first cytology and subsequent histopathology diagnosis (NKCx). After adjusting for birth cohort, the PPV of high-grade cytology for CIN2+ was 69.9% (95 percent CI, 67.9–71.9), 64.9 percent (95 percent CI, 59.8–69.8), and 57.4 percent (95 percent CI, 50.9–63.7) among women unvaccinated, initiating vaccination at age 17–22 years, and initiating vaccination before age 17 years, respectively, corresponding to a reduction The PPV of cytology for CIN2+ reduced in vaccinated women, and the drop was more pronounced in girls who were vaccinated at a younger age. A transition from cytology to HPV testing could help to improve screening results.

In 2020 Yu Huang et al., [47] 549 female patients who had visited a physical examination clinic were investigated retrospectively. The MSP data was gathered, and tests for vaginal microecology, HPV, and cervical conization pathology (CCP) were conducted as needed.

Patients with varying degrees of BV severity had variable MSP status. Furthermore, the HPV positive ratio increased as the severity of BV worsened. MSP, on the other hand, was linked to a positive Human papillomavirus result, including Human papillomavirus 16, HPV 18, and other high-risk Human papillomavirus infections. The MSP group had a larger percentage of CCP outcomes that were good (particularly cases with CIN II and CIN III). Similarly, a higher BV severity meant a faster progression of CIN/CC. To predict the CCP outcome, a logistic regression model based on age, MSP status, and Nugent score level was utilized. Furthermore, the area under the curve for a receiver operating characteristic curve study was 0.834.

Jonah Musa et al., [48] In Nigerian 2020, researchers studied HIV with the development of epithelial cell abnormalities in women who had previously had normal cervical cytology. A total of 1599 women were included in the study. Overall, 3.7 percent of women (57/1556) reported having HIV. At the time of the first Pap, the median age was 39 years (IQR: 33–45). HIV-positive women were younger (36.3 8.1) than HIV-negative women (39.3 6.6), p = 0.005. After 3809 person-years (PYs) of follow-up, 243 women (15%) developed an ECA, with an incident rate of 6.38 per 100 PYs. In both unadjusted (7.4 per 100 PYs vs 6.4 per 100 PYs, HR = 1.17; 95 percent CI: 0.53, 2.3) and adjusted analyses (aHR = 1.78; 95 percent CI: 0.87, 3.65), HIV status was not significantly linked with developing ECA.

In 2019 Nidhi Singh and Hanslata Gehlot [49] Cervical cytology was studied in females over the age of 21. The majority of patients (52.4%) were from rural areas and were of lower socioeconomic status (30.2 percent). In 84.2 percent of cases, there was multiparity. White discharge was the most prevalent presenting complaint (46.8 percent). On Pap smear, the most common type was inflammatory smear (91.4%), followed by ASCUS, 1.2 percent AGC, 1.4 percent LSIL, 1% HSIL, and 0.4 percent SCC. Cervical cytology is a valuable tool for detecting

premalignant and cancerous cervix lesions early. In vulnerable age groups, pap smear screening should be done on a regular basis.

Luana Taís H. Backes et al., [50], Only 114 (22.8 percent) of the participants had the squamocolumnar junction (SCJ) sampled, and their occurrence reduced with increasing age (p 0.001). The majority of smears (95.6%) were classed as atrophic. The majority of the lactobacillus flora was found in the 22 non-atrophic smears, according to microbiological examination. Cocci were the most common flora in atrophic swabs, accounting for 47.2 percent. Only 4% of the cases had cytological changes: atypical squamous cells of undetermined significance (ASC-US) – eight cases/40 percent; atypical squamous cells – cannot exclude high-grade squamous intraepithelial lesion (ASC-H) – five cases/25 percent; high-grade squamous intraepithelial lesion (HSIL) – three/15 percent; low-grade squam Four (20%) of the modified smears included SCJ cells, and four (20%) of the patients took hormones (two cases of ASC-H (10%) and two cases of ASC-US (10%), indicating a link between the development of the lesion and the use of hormones (p 0.05).

S. Senthil Priya and R. Shankar [51] A prospective research published in 2018 revealed that 26% of the subjects had inflammatory pap smear, 66 percent were negative for intraepithelial lesion, and only 1% of the subjects had signs of carcinoma cervix, with one patient having Atypical Squamous Cell of Undetermined Significance (ASCUS) and another patient having Low-grade Squamous Intraepithelial Lesion (LSIL), and only 6% of the subjects had no satisfactory sample. The authors of this study discovered a statistically significant link between the age at marriage and the pap smear report, with the lower the age at marriage (less than 20 years) higher incidence of inflammatory changes in the cervix and both patients with ASCUS and LSIL were between the ages of 15 and 16 years.

Gudrun Broberg et al., [52] Women with low disposable family income (adjOR 2.06; 95 percent confidence interval (CI) 2.01 2.11), poor education (adjOR 1.77; CI 1.731.81), and not cohabiting (adjOR 1.47; CI 1.451.50) were more likely to skip cervical screening, according to a study published in 2018. Being unemployed and receiving welfare benefits were also significant variables in non-attendance. Screening programs are conducted by Swedish counties, and the adjusted odds ratios for non-participation in counties ranged from OR 4.21 (CI 4.064.35) to OR 0.54 (CI 0.520.57) when compared to the reference county. In the unadjusted study, being born outside of Sweden was a risk factor for non-attendance, but this decreased in certain significant groups after socioeconomic considerations were taken into account.

Dawit Wolday et al., [53] in a 2018 study, 92 (39.5%) of the 233 study participants had abnormal cytology. Only 48.9% of women with abnormal cervical cytology had positive HPV DNA, compared to 100% of those with normal cytology. The prevalence of high-risk (HR)-Human papillomavirus was 83.2 percent in these women, and it was substantially greater in women with abnormal cervical cytology (92.4 percent vs. 71 percent, p 0.0001) than in women with normal cytology. Human papillomavirus 16 (44.1%) was the most frequently discovered genotype, followed by HPV35 and Human papillomavirus 45 (both 6.2%), HPV56 (3.7%), HPV31 (4.4%), Human papillomavirus 18 and HPV59 (both 3.1%), HPV58 (2.5%), and HPV39 (2.5%). (1.9 percent). While Human papillomavirus 16 (20.3 percent), HPV35 (8.7%), HPV56 and HPV58 (each 5.8%), HPV31, HPV18, and HPV39 (each 4.4 percent), HPV45 (2.9 percent), and Human papillomavirus 59 and HPV68 (each 1.5 percent) were the most common HR-HPV infections in women with normal cytology, the most common HR-HPV infections in women with abnormal cytology were Human papillomavirus 16 (62 percent), HPV45 (8.7% (each 2.2 percent). In women with normal or abnormal cytology, we found a low frequency of multiple

HPV infections. Living in a rural region (OR 3.24, 95 percent CI: 1.13–9.30), being multipara (OR 7.35, 95 percent CI: 1.78–30.38), and having abnormal cervical cytology results (OR 6.75, 95 percent CI: 1.78–25.57) were all independently linked with Human papillomavirus 16 genotype, according to multivariable logistic analysis.

Jian-Hong Fang et al. [54], On the basis of humanpapillomavirus infection investigations, researchers looked into the effect of smoking on high-grade cervical cancer in women in 2018. Long-term (more than 8 years) and heavy (18 or more cigarettes per day) smokers are highly responsible for the increased incidence of CIN3 or CIN3+ among high-risk HPV positive women. Heavy smoking increased the probability of CIN3+ in women with persistent HPV infection compared to women who never smoked (HR, 2.31; 95 percent CI, and 1.12–4.16). In persistently high-risk HPV-infected women, smoking increases the risk of high-grade cervical lesions. This helps to clarify the significance of smoking in cervical cancer.

In 2018 Pushp Lata Sachan et al., [55] a cervical cancer screening using the pap smear test and clinical correlation was investigated. The majority of the women were multiparous and in their 30s–50s. The most prevalent complaint was vaginal discharge, which was reported by 36.96 percent of the women. 12.78 percent of women had an irregular menstrual cycle, and 25.63 percent had abdominal pain, while 15.15 percent were asymptomatic. 93.57 percent of the women had an adequate Pap smear test, while 6.42 percent of the women had an unsatisfactory sample. In 48.84 percent of cases, the test came back clear for cancer, while 42.66 percent showed infection or inflammation. In 2.90 percent, 5.09 percent, and 0.48 percent, respectively, atypical squamous cells of unknown significance, low grade squamous intraepithelial lesion (LSIL), and high grade squamous intraepithelial lesion were found. ASCUS, LSIL, and HSIL positive Pap tests were subjected to a colposcopy and guided biopsy. Women have had an

abnormal Pap test should get a colposcopy, and those who have had an abnormal colposcopy should get a biopsy. In a gynecological patient, a Pap smear is a simple, noninvasive, cost-effective, and uncomplicated procedure for detecting precancerous lesions.

Adepiti Clement Akinfolarin et al., [56] in 2017, the average age of women was 45.77 9.9 years, with a median age of 50 years. 728 (40.6 percent) women had a normal Pap smear test. Only 20 ladies have had more than one Papsmear procedure. Inflammatory smear results were the most prevalent abnormality, with 613 women (29.9%) reporting it. Atypical squamous cell of unknown importance, low grade squamous intraepithelial lesion (LGSIL), and high grade squamous intraepithelial lesion (HGSIL) were all found in 117 (5.7%), 209 (10.2%), and 111 (5.4%) of the women, respectively. Squamous cell carcinoma and atypical glandular cell carcinoma were found in 12 (6.0%) and 3 (1.0%) cases, respectively. In this context, abnormal Pap smears are common and women begin cervical cancer screening late in their reproductive lives, well after the peak age for cervical premalignant lesions.

Shu Chen et al.[57], The link between diabetes/hyperglycemia and the prognosis of cervical cancer patients was explored in a comprehensive analysis published in 2017. Diabetes was linked to a lower overall survival rate (HR=1.59, 95 percent CI: 1.35–1.87, P.001) and a lower recurrence-free survival rate (HR=1.98, 95 percent CI: 1.47–2.66, P.001) in cervical cancer patients, according to the study. Diabetes was also independently linked with poor overall survival (HR=1.69, 95 percent CI: 1.38–2.05, P.001) and poor recurrence-free survival (HR=1.98, 95 percent CI: 1.47–2.66, P.001) in cervical cancer patients, according to a meta-analysis of adjusted HRs.

Mette T. Roensbo et al., [58], In 2017, researchers looked at 94 cases, 60 of which were RTRs and 60 of which were BMTRs. The overall prevalence of high-risk Human papillomavirus was 15.0 percent [95 percent confidence interval (CI) 7.1–26.6], with BMTR (29.4 percent, 95 percent CI 10.3–56.0) having a greater prevalence than RTR (9.3 percent, 95 percent CI 2.6–22.1), albeit this was not statistically significant (p = 0.10). High-risk Human papillomavirus was found across a wide range of genotypes, with HPV 45 being the most frequent (3.3 percent). High-risk HPV strains included in bivalent/ quadrivalent and nonavalent vaccines had prevalences of 1.7 and 8.3 percent, respectively. Low-grade and high-grade cytological abnormalities were seen in 6.7 and 5.0 percent of the participants, respectively. Conclusions. Immunocompromised women were infected with a wide variety of high-risk Human papillomavirus genotypes, with a higher prevalence of cytological abnormalities than previously reported in general population investigations. When compared to bivalent/quadrivalent HPV vaccines, the nonavalent Human papillomavirus vaccine will provide superior protection against HPV-related diseases for immunocompromised patients.

Emma Foster et al., [59], the year 2017 was investigated. Irritable bowel disease (2,683), psoriatic and enteropathic arthropathies (1,848), rheumatoid arthritis (1,246), multiple sclerosis (MS) (1,426), systemic lupus erythematosus and/or mixed connective tissue disease (SLE/MCTD) (702), HIV (44), and 985,383 immunocompetent controls were included in the study. When compared to controls, the SLE/MCTD and Human papillomavirus groups had higher incidences of high-grade histological and cytological abnormalities. With the exception of the MS group, all females with AICs had higher frequencies of low-grade cytological abnormalities. High-grade cervical abnormalities are more common in women with SLE/MCTD or HIV. Most females with AICs have a higher rate of low-grade dysplasia, which is associated

with increased HPV infection. These findings suggest that cervical cancer prevention efforts should be expanded to reach these at-risk women.

Umarani MK et al., [60] during the time period in question, 1418 cases were investigated, according to a 2016 report. The women's ages ranged from 16 to 92. The most common complaint was vaginal irregular bleeding and leucorrhea. 1164 smears (82.08%) were in the NILM group, while 132 smears (9.3%) were unsuitable for evaluation. ASCUS was responsible for 4.87 percent of cases, ASC-H for 0.56 percent, LSIL for 1.62 percent, HSIL for 0.64 percent, AGC for 0.64 percent, and SCC for 0.28 percent.

A case control study was done by Leonard Ogbonna Ajah et al. [61], in 2016, seven (4.5%) and two (1.3%) of IUD users, respectively, experienced Cervical Intraepithelial Neoplasia (CIN) 1 and CIN 2. In addition, CIN 1 and CIN 2 were found in 5 (3.2%) and 1 (0.6%) of non-users of contemporary contraception, respectively. Cervical neoplasia was found to be present in 4.8 percent of the subjects. Although there was a higher proportion of women with CIN among IUD users than among non-users of contemporary contraception, the difference was not statistically significant.

Mojgan Karimi-zarchi et al., [62] in 2015 reported that patients with rheumatoid arthritis (53.3 percent) had the highest rate of immunodeficiency, followed by patients undergoing chemotherapy (30.7 percent), patients with lupus erythematosus (12.9 percent), and patients with AIDS (12.9 percent) (3 percent). For colposcopy, the results were 66.7, 98.94, 80, 97.9, and 97 percent, respectively. Colposcopy had higher accuracy, sensitivity, specificity, and negative predictive values than the Pap test in detecting high-grade, cervical, pre-malignant lesions

(cervical intraepithelial neoplasia: CIN 2) than the Pap smear. As a result, instead of a Pap smear, secondary immunodeficient patients should get an annual colposcopy.

In 2015 Essaada Belglaia et al., [63] studied a Women were 42 years old (18–76 years old) on average. The prevalence of HIV was 36.2 percent. The prevalence of any Human papillomavirus type was 23.7 percent in the study population, with Human papillomavirus negative women (13.3 percent) having a lower frequency than HIV-positive women (39.3 percent). The most common type was Human papillomavirus 16 (6.5 percent), followed by Human papillomavirus 53 and HPV74 (3.4 percent each). The majority of women had normal cervical smears (82%) and the others were diagnosed with LGSIL (13%) and HGSIL (3%). (5 percent). In 17.4 percent of normal smears, 43.4 percent of LGSIL, and 75 percent of HGSIL, HPV was found. Independent of socio-demographic and behavioral risk factors, HIV status was the most powerful predictor of high risk (hr) and probable hr (phr) HPV infection (odds ratio 4.16, 95 percent confidence interval 1.87–9.24, p = 0.0005), followed by abnormal cytology (OR 3.98, 95 percent confidence interval 1.39–11.40, p = 0.01). Human papillomavirus infections are often found in a Moroccan hospital-based population in the Souss area. Furthermore, among HIV-positive women, a high prevalence of hr and phrHPVs, as well as precancerous lesions, is likely linked to an elevated risk of cervical cancer.

In 2014, Hui Jun Chih et al. [64], Condom and oral contraceptive use and the risk of cervical intraepithelial neoplasia in Australian women: a measured cross-sectional study CIN was found to be prevalent in 15.8% of people. Women with abnormal Papanicolaou (Pap) smear results indicating CIN had a substantially shorter duration of oral contraceptive use than women without abnormal Pap smear results (meanSD, 5.65.2 years vs. 8.27.2 years; p=0.002). When compared to 3 years of use, oral contraceptive use for 10 years lowered the risk of CIN (p=0.012).

However, after controlling for confounding factors, the use of a condom for contraception may not be related with a lower incidence of CIN (adjusted OR, 0.52; 95 percent CI, 0.05 to 5.11; p=0.577). The use of oral contraceptives for contraception, but not condoms, proved to be inversely related to CIN. Long-term usage of an oral contraceptive has been shown to reduce the risk of CIN.

Rana Al-Awadhi et al., [65] in 2013, HPV DNA was found in 152 women (51%) with 29 different Human papillomavirus genotypes, including 16 high-risk (HR) genotypes (16, 18, 31, 33, 35, 39, 45, 51, 53, 56, 58, 59, 66, 68, 73, 97). HPV16 was the most common virus (24.3 percent), followed by Human papillomavirus 11 (13.8 percent), HPV66 (11.2 percent), HPV33 (9.9%), Human papillomavirus 53 (9.2%), HPV81 (9.2%), HPV56 (7.9%), and HPV18 (7.9%). (6.6 percent). In women with invasive cervical cancer (ICC), high-grade squamous intraepithelial lesion (HSIL), and low-grade squamous intraepithelial lesion (LSIL), Human papillomavirus prevalence was 86, 67, and 89 percent, respectively. In terms of age distribution, women aged 20 to 29 years detected 69 percent of all HPVs, and the HPV incidence rate decreased with age. As the severity of the cytological diagnosis grew, the proportion of single infections reduced, while the number of multiple infections increased.

Kevin P McKenzie et al. [66] conducted a prevalence analysis in 2011. 267 women out of 595 who were eligible received Pap testing and had available cytology findings, with 258 (97%) on a non-nucleoside reverse transcriptase inhibitor (NNRTI)-based regimen. Antiretroviral medication was used for an average of 13 months [interquartile range (IQR), 8-19]. 123 women (46%) had abnormal cytology, with 70 (26%) having low grade squamous intraepithelial lesions (LSIL), 22 (8%) having high grade squamous intraepithelial lesions (HSIL), 30 (11%) having atypical squamous cells of uncertain significance (ASCUS), and 1

(0.4%) having atypical glandular cells (AGC). Women with SIL had a lower median CD4 cell count (239 vs 287 cells/mm3; P=0.02), lower income (70 USD per month: 57 percent vs 38 percent; P=0.01), and less regular condom use (24 percent vs 40 percent; P=0.02). The length of time on an antiretroviral regimen and the type of antiretroviral regimen had no bearing on SIL.

In 2010 Changdong Li et al., [67] studied the prevalence of cervical lesions diagnosed by histology was 5.8%. The total prevalence of high-risk HPV was 9.9%, with 50.5 percent having a cervical lesion and 7.4 percent not having a cervical lesion. The amount of high-risk HPV DNA in the blood rose as the severity of the lesions increased. HPV 16 was the most common type among women with cervical lesions (26.5%), followed by HPV 58 (8.8%), HPV 33 (7.8%), and HPV 56 (7.8%). (5.3 percent). More risk factors for HPV infection were women under 50 years old, marital status, pregnancy and delivery status, couple's sexual conduct, contraception history, columnar ectopy, and bacterial vaginosis or trichomonas vaginitis history. Cervical lesion factors were similar, although all correlations were decreased when compared to HPV infection. Only middle-aged women, their husbands' sexual partners, oral contraceptives, columnar ectopy, and trichomonas vaginitis history were found to be linked to cervical lesion.

Dania Al-Jaroudi, Tasnim Z. Hussain [68] in 2010 reported that In 166 of 241 individuals (67.9%), the Pap smear was normal, abnormal in 71 (29.5%), and unacceptable for evaluation in four (1.7 percent). Epithelial cell abnormalities was observed in 7 (2.9 percent) patients, inflammation in 55 (22.8 percent), and infection in 9 (3.7 percent) patients, according to the revised Bethesda system. Atypical squamous cells of undetermined significance (42.8 percent), atypical squamous cells of high grade (ASC-H) (n=1, 14.3 percent), low-grade squamous intraepithelial lesion (LSIL) (n=2, 28.5 percent), and glandular cell abnormalities (AGS) (n=1, 14.3 percent) were the four types of epithelial cell abnormalities.

AIMS AND OBJECTIVES

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- To determine the association of HPV infection in women with abnormal cervical cytology.

MATERIALS AND METHODS

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Title

Association of HPV infection in women with abnormal cervical cytology

Source of data

Women coming to gynecology OP in Department of Obstetrics and Gynaecology, attached to Madurai Medical College, Madurai

Methods of collection of data

- **Study Design:** Cross sectional study
- **Study Period:** 1year
- **Sample Design:** random sample
- **Sample Size:** 50

Inclusion Criteria

1. Women ages 30 to 65 Years.
2. Pap smear showing abnormal cervical cytology

Exclusion Criteria

1. Women of age <30 and >65
2. Proven Ca cervix
3. Women with normal cervical cytology
4. Unwillingness to give informed consent.

METHODOLOGY

Samples were taken from the cervical squamous columnar junction area using a cervical brush or pap smear rod and the exfoliated cells were placed into Preserve Cyt media. Cervical slides were prepared and the cytological classifications were made according to Bethesda 2001 criteria .Residual exfoliated cells from Preserve Cyt media were used for HPV testing by ELISA.

Statistical analysis: Statistical analysis was performed using IBM SPSS version 22.0 (Statistical Package for Social Sciences).

The prevalence of HPV positivity was assessed using the chi-square test. A p-value of less than 0.05 was considered significant. Odd ratios (OR) for HPV positivity were calculated with their 95% confidence intervals**.**

RESULTS AND ANALYSIS

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Table 1: Age distribution of the women with abnormal cervical cytology

(N=50)

Age (Years)	Frequency (n)	Percentage (%)
21-30	1	2
31-40	11	22
41-50	27	54
51-60	11	22
Total	50	100

Table 1a: Mean age distribution of the women with abnormal cervical cytology

N	Mean (Years)	Median (years)	Standard deviation	Minimum (years)	Maximum (years)
50	44.14	44	7.502	30	60

(Table and figure 1 and 1a) Among the total 50 women with abnormal cervical cytology, 54% (n=27) of the patients were in the age group ranging between 41-50 years with the mean age of the patients was observed as 44.14 ± 7.502 (years).

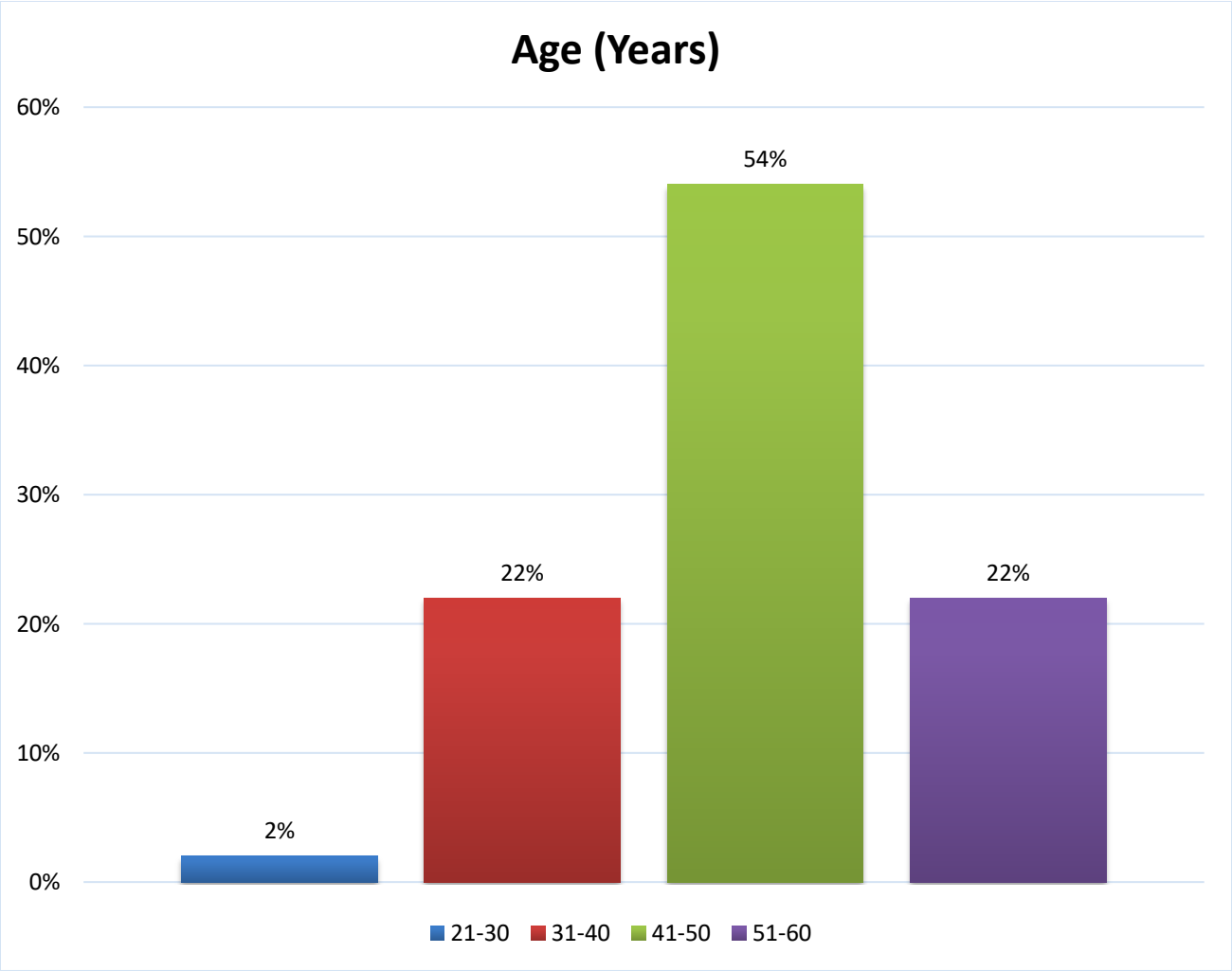
Age (Years)
60%
50%
40%
30%
20%
10%
0%
2%
22%
54%
22%
21-30
31-40
41-50
51-60

Table 2: Parity distribution of the women with abnormal cervical cytology

(N=50)

Parity	Frequency (n)	Percentage (%)
P1L1	2	4.0
P1L2	1	2.0
P2L0	1	2.0
P2L1A1	1	2.0
P2L2	25	50.0
P2L2A1	3	6.0
P2L2A2	2	4.0
P2L2A3	1	2.0
P2L3	3	6.0
P3L2	1	2.0
P3L3	2	4.0
P4L2	3	6.0
P4L3	2	4.0
P4L4	1	2.0

P5L3	1	2.0
P6L3	1	2.0
Total	50	100.0

From (Table 2) we infer that, among 50 women with abnormal cervical cytology, 50% (n=25) of patients had P2L2 Parity

Table 3: Age at marriage distribution of the women with abnormal cervical cytology

(N=50)

Age at marriage (Years)	**Frequency (n)**	**Percentage (%)**
Less than 18 years	17	34
More than 18 years	33	66
Total	50	100

Table 3a: Mean age at marriage distribution of the women with abnormal cervical cytology

N	Mean (Years)	Median (years)	Standard deviation	Minimum (years)	Maximum (years)
50	18.34	18	1.624	15	22

(Table 3 and 3a) Among the total 50 women with abnormal cervical cytology, 66% (n=33) of the patients were more than 18 years at marriage with the mean age of the patients was observed as 18.34 ± 1.624 (years).

Table 4: Distribution based on socio economic status among women with abnormal cervical cytology (N=50)

Socio economic status	Frequency (n)	Percentage (%)
Lower	43	86
Upper lower	7	14
Total	50	100

(Table 4) It was observed that, most of the women with abnormal cervical cytology, 43 (86%) had lower socio economic status.

Table 5: Distribution based on multiple sexual partners among women with abnormal cervical cytology (N=50)

Multiple sexual partners	Frequency (n)	Percentage (%)
No	48	96
Yes (2nd marriage)	2	4
Total	50	100

(Table and figure 5) It was observed that, most of the women with abnormal cervical cytology, 48 (96%) had no multiple sexual partners.

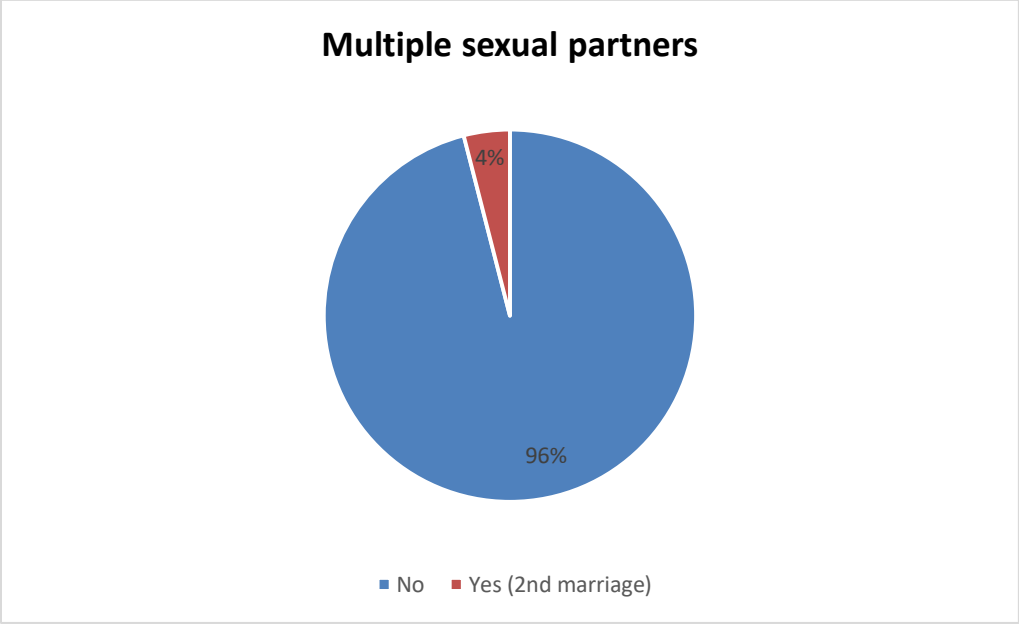

Table 6: Distribution based on partners with multiple sexual partners among women with abnormal cervical cytology (N=50)

Partners with multiple sexual partners	Frequency (n)	Percentage (%)
No	49	98
Yes	1	2
Total	50	100

(Table 6) It was observed that, most of the women with abnormal cervical cytology, 49 (98%) had no partners with multiple sexual partners.

Table 7: Distribution based on history of STI among women with abnormal cervical cytology (N=50)

History of STI	Frequency (n)	Percentage (%)
No	43	86
Yes	7	14
Total	50	100

(Table and figure 7) It were observed that, most of the women with abnormal cervical cytology, 43 (86%) had no history of STI.

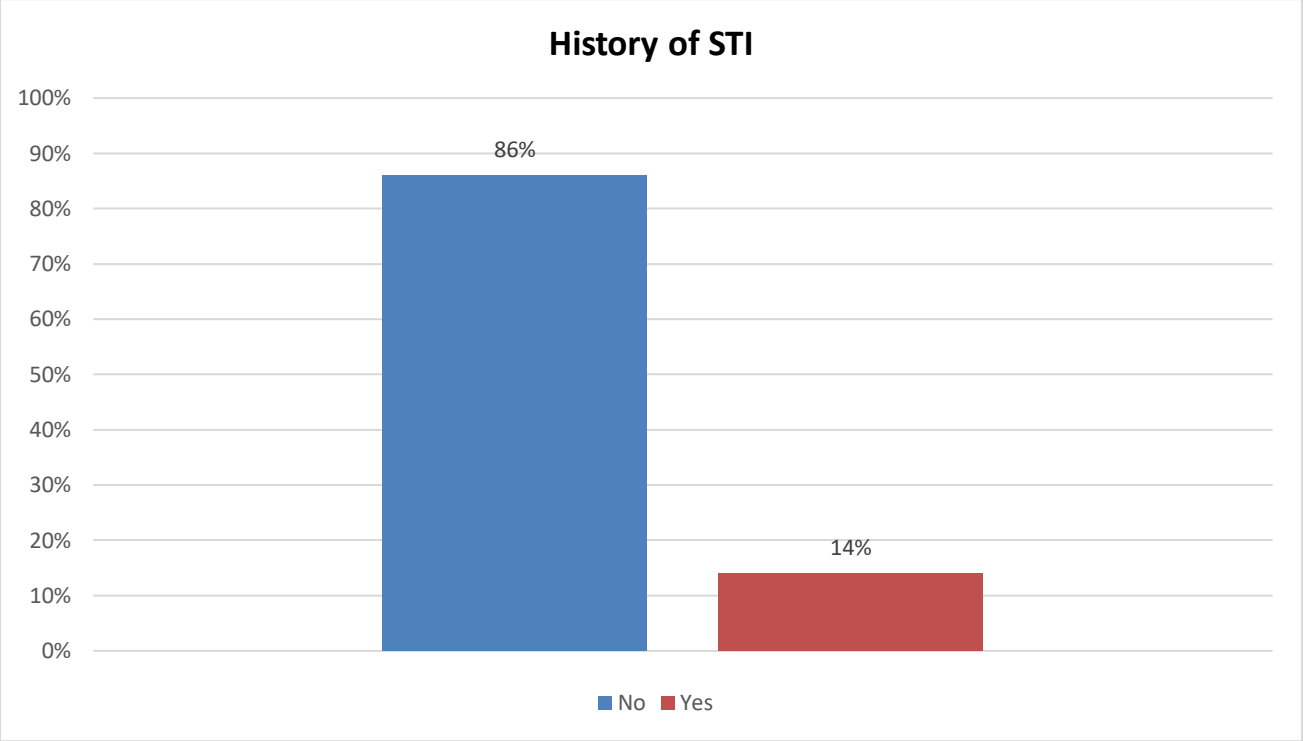

Table 8: Distribution based on history of previous HPV infection among women with abnormal cervical cytology (N=50)

History of previous HPV infection	Frequency (n)	Percentage (%)
No	50	100
Yes	0	0
Total	50	100

(Table 8) It was observed that, all of the women with abnormal cervical cytology, 50 (100%) had no history of previous HPV infection.

Table 9: Distribution based on use of condoms among women with abnormal cervical cytology (N=50)

Use of condoms	Frequency (n)	Percentage (%)
No	34	68
Yes	16	32
Total	50	100

(Table 9) It was observed that, most of the women with abnormal cervical cytology, 34 (68%) had no use of condoms.

Table 10: Distribution based on use of IUCD among women with abnormal cervical cytology (N=50)

Use of IUCD	Frequency (n)	Percentage (%)
No	32	64
Yes	18	36
Total	50	100

(Table 10) It was observed that, most of the women with abnormal cervical cytology, 32 (64%) had no Use of IUCD.

Table 11: Distribution based on use of OCP among women with abnormal cervical cytology

(N=50)

Use of OCP	Frequency (n)	Percentage (%)
No	46	92
Yes	4	8
Total	50	100

(Table 11) It was observed that, most of the women with abnormal cervical cytology, 46 (92%) had no use of OCP.

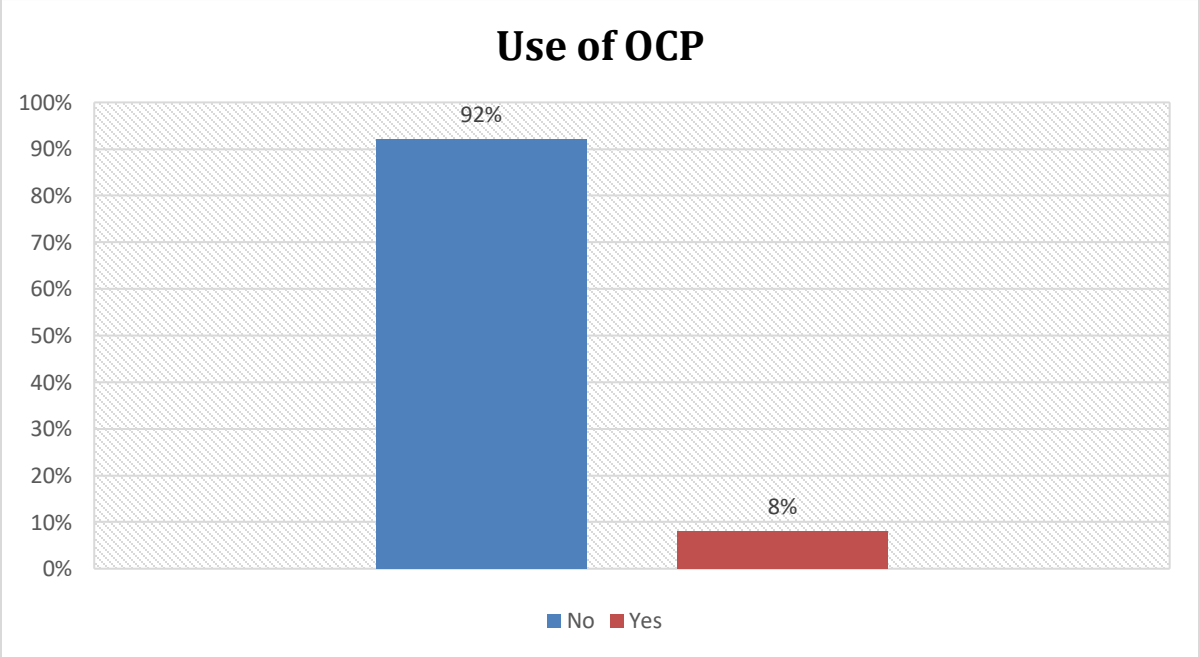

Table 12: Distribution based on hormone replacement therapy among women with abnormal cervical cytology (N=50)

Hormone replacement therapy	Frequency (n)	Percentage (%)
No	50	100
Yes	0	0
Total	50	100

(Table 12) It was observed that, all of the women with abnormal cervical cytology, 50 (100%) had no hormone replacement therapy.

Table 13: Distribution based on HIV among women with abnormal cervical cytology

(N=50)

HIV	Frequency (n)	Percentage (%)
No	50	100
Yes	0	0
Total	50	100

(Table 13) It was observed that, all of the women with abnormal cervical cytology, 50 (100%) had no HIV.

Table 14: Distribution based on diabetic mellitus among women with abnormal cervical cytology (N=50)

Diabetic mellitus	Frequency (n)	ercentage (%)
No	33	66
Yes	17	34
Total	50	100

(Table 14) It was observed that, most of the women with abnormal cervical cytology, 17(34%) had diabetic mellitus.

Table 15: Distribution based on immune suppressive agents among women with abnormal cervical cytology

(N=50)

Immune suppressive agents	Frequency (n)	Percentage (%)
No	33	66
Yes	17	34
Total	50	100

(Table and figure 15) It was observed that, most of the women with abnormal cervical cytology, 17 (34%) had immune suppressive agents.

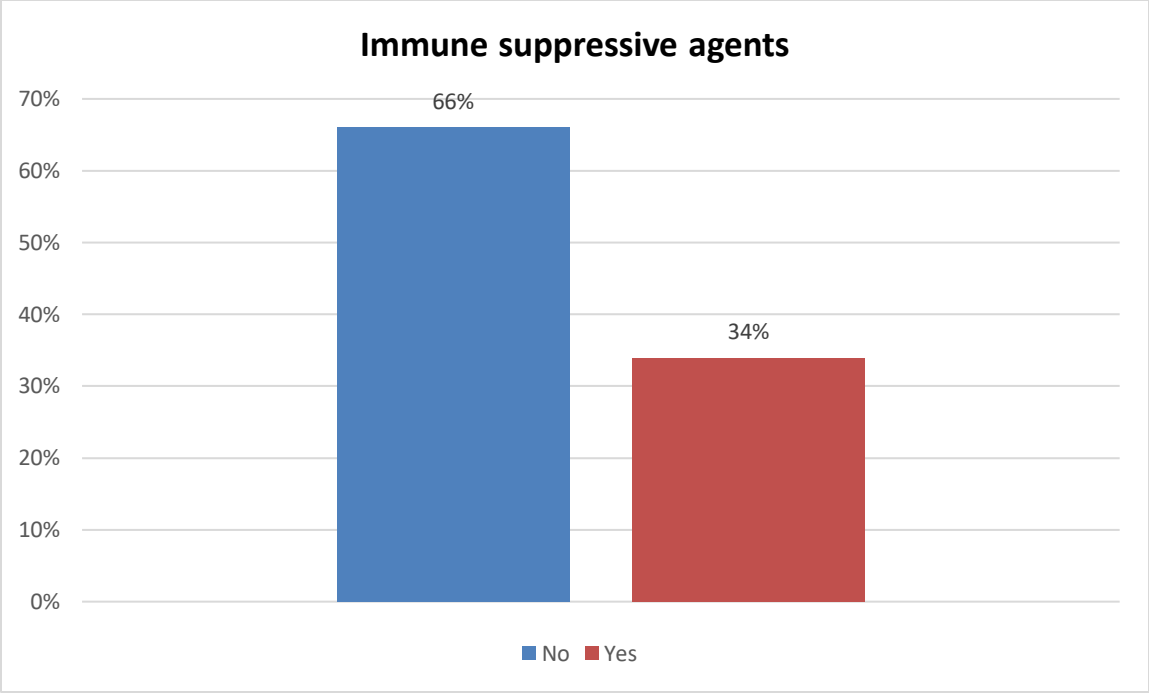

Table 16: Distribution based on smoking habits among women with abnormal cervical cytology (N=50)

Smoking habits	Frequency (n)	Percentage (%)
No	50	100
Yes	0	0
Total	50	100

(Table 16) It was observed that, all the women with abnormal cervical cytology, 50 (100%) had no smoking habits.

Table 17: Distribution based on auto immune disorder among women with abnormal cervical cytology (N=50)

Auto immune disorder	Frequency (n)	Percentage (%)
No	50	100
Yes	0	0
Total	50	100

(Table 17) 50 (100%) had no auto immune disorder.

Table 18: Distribution based on complaints among women with abnormal cervical cytology

(N=50)

Complaints	Frequency (n)	Percentage (%)
No	20	40
Yes	30	60
Total	50	100

(Table and figure 18) It was observed that, most of the women with abnormal cervical cytology, (60%) had complaints.

30

Table 19: Distribution based on HPV vaccination status among women with abnormal cervical cytology (N=50)

HPV vaccination status	Frequency (n)	Percentage (%)
No	50	100
Yes	0	0
Total	50	100

(Table 19) It was observed that, all the women with abnormal cervical cytology, 50 (100%) had no HPV vaccination status.

Table 20: Distribution based on history of cervical cancer screening by pap smear among women with abnormal cervical cytology (N=50)

History of cervical cancer screening by pap smear	Frequency (n)	Percentage (%)
No	44	88
Yes	6	12
Total	50	100

(Table and figure 20) It was observed that, most of the women with abnormal cervical cytology, 44 (88%) had no history of cervical cancer screening by Pap smear.

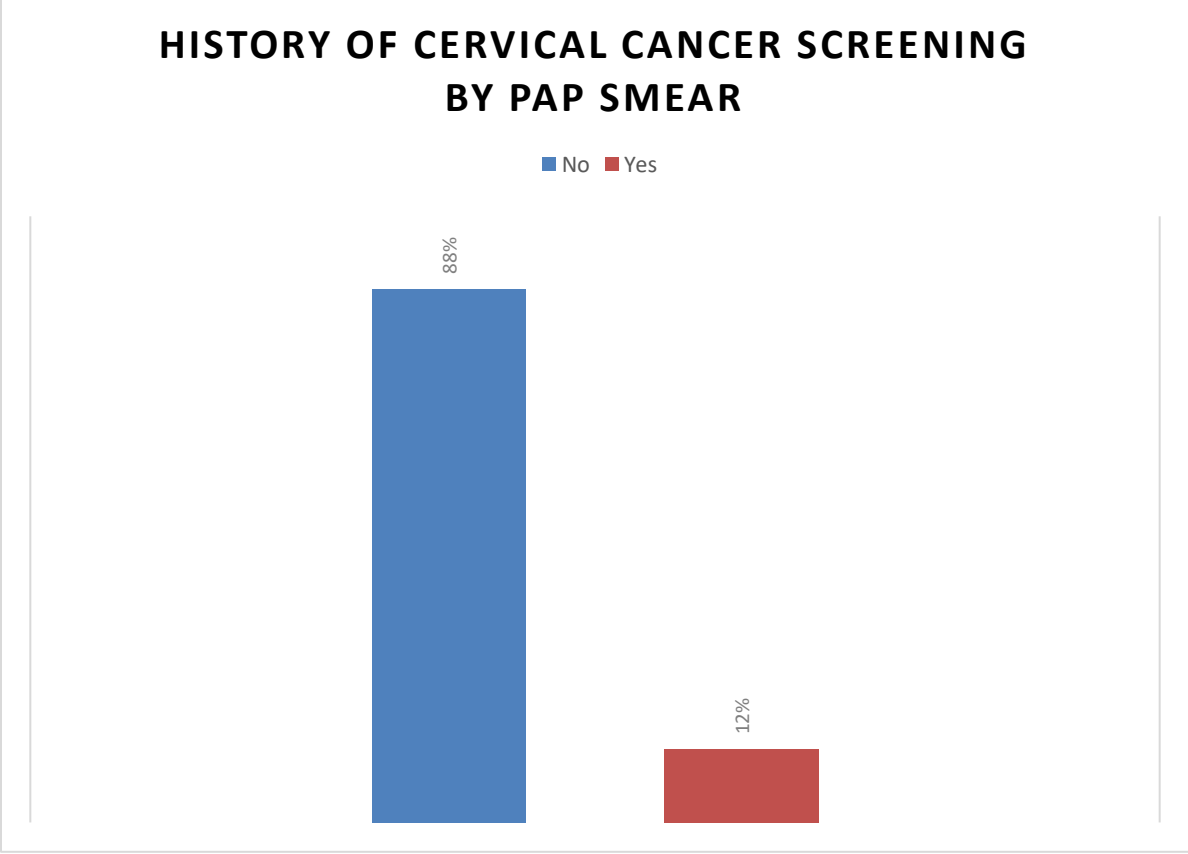

Table 21: Distribution based on history of colposcopy screening among women with abnormal cervical cytology

(N=50)

History of colposcopy screening	Frequency (n)	Percentage (%)
No	49	98
Yes	1	2
Total	50	100

(Table and figure 21) It was observed that, most of the women with abnormal cervical cytology, 49 (98%) had no history of colposcopy screening.

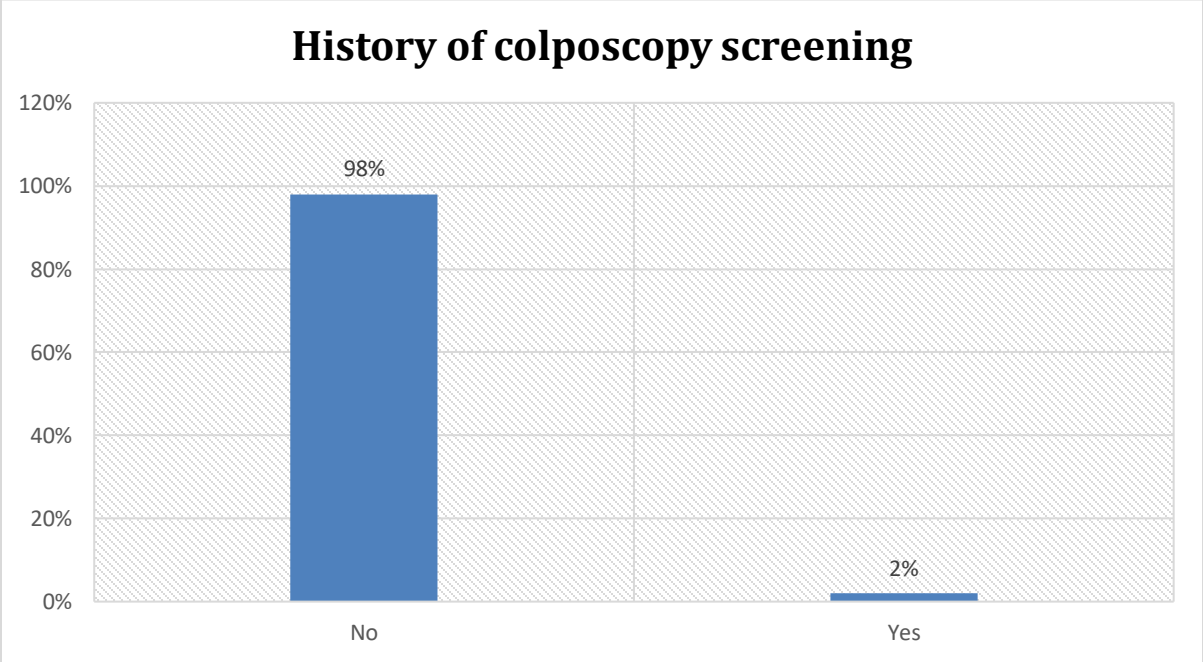

Table 22: Distribution based on history of testing of HPV among women with abnormal cervical cytology

(N=50)

History of testing of HPV	Frequency (n)	Percentage (%)
No	50	100
Yes	0	0
Total	50	100

(Table 22) It was observed that, all of the women with abnormal cervical cytology, 50 (100%) had no history of testing of HPV.

Table 23: Distribution based on Bethesda classification among women with abnormal cervical cytology (N=50)

Bethesda classification	Frequency (n)	Percentage (%)
ASCUS	7	14
HSIL	14	28
LSIL	29	58
Total	50	100

(Table 23) It was observed that, most of the women with abnormal cervical cytology, 29 (58%) had LSIL of Bethesda classification.

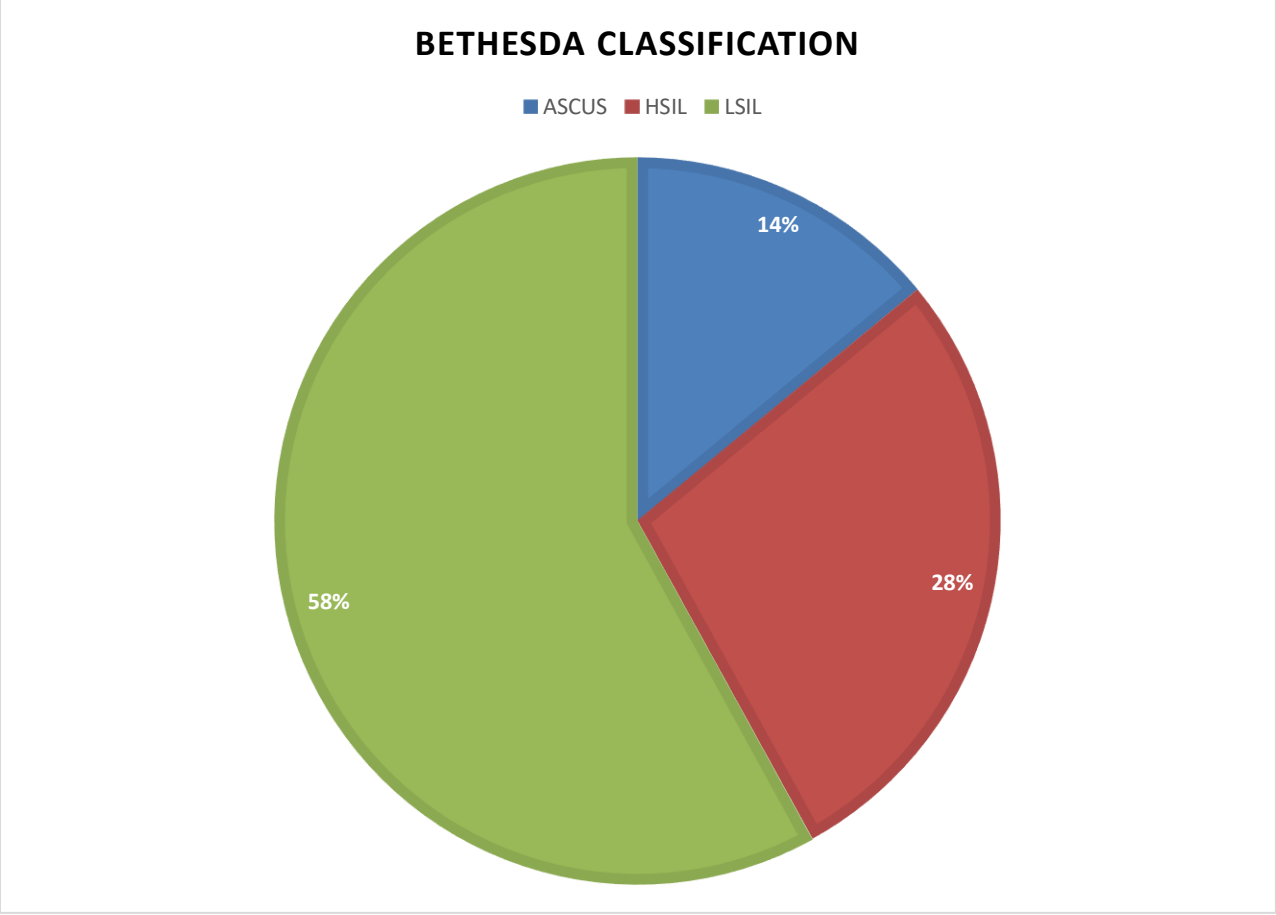

Table 24: Distribution based on HPV testing among women with abnormal cervical cytology (N=50)

HPV testing	Frequency (n)	Percentage (%)
Negative	40	80
Positive	10	20
Total	50	100

(Table 24) It was observed that, most of the women with abnormal cervical cytology, 10 (20%) had positive HPV testing.

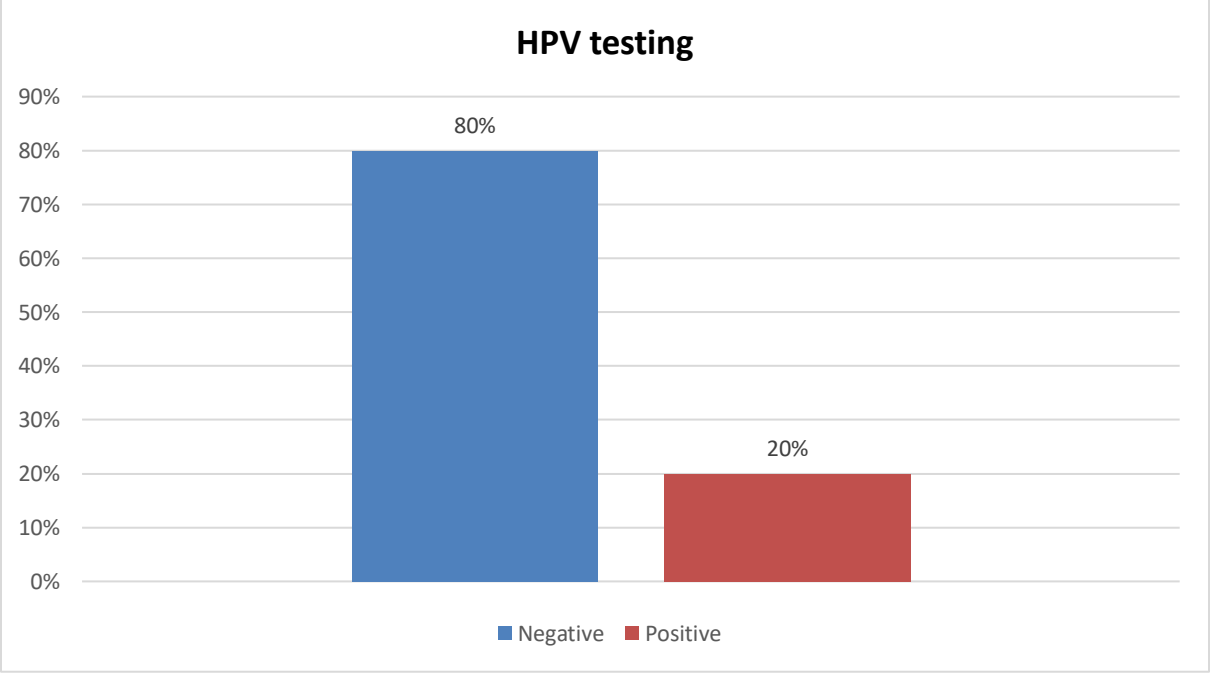

Table 25: Association of HPV infection with Bethesda classification among women with abnormal cervical cytology.

(N=50)

Bethesda classification	**HPV infection**				**STATISTICAL SIGNIFICANCE**
	NEGATIVE		**POSITIVE**		
	N	**%**	**N**	**%**	
ASCUS	3	7.5	4	40	X^2 =9.791 df =2 **p-value =0.007* S**
HSIL	10	25	4	40	
LSIL	27	67.5	2	20	

-p < 0.05 significant

The table 25 reveals the statistically significant association of HPV infection with Bethesda classification among women with abnormal cervical cytology with chi-square value of **(χ^2=9.791, d.f=2) at** p<0.05 level.

DISCUSSION

DISCUSSION

Cervical cancer is the fourth most common cancer worldwide and human papillomavirus (HPV) is a major etiological agent during its development.

In our study we are trying to give the data in association of HPV infection in women with abnormal cervical cytology.

In the present study 50 patients with abnormal cervvical cytology who came to gynecology OP were selected during the study period.

Among the total 50 women with abnormal cervical cytology, 54% of the patients were in the age group ranging between 41-50 years followed that 11% of the patients were in the age group ranging between 31-40 years and 51-60 years with the mean age of the patients was observed as 44.14 ± 7.502 (years).

Similarly, R Adepiti Clement Akinfolarin in 2017[56] documented that The mean age of the women was 45.77 ± 9.9 years and the mode was 50 years.

In regards to Parity, among 50 women with abnormal cervical cytology, 50% of patients had P2L2 Parity. This was similar to a study by S. Senthil Priya and R. Shankar[51] states that primi (42.5%) followed by 2nd gravida (37.5%) and only 7% of were in the 4th gravida. Another study shows 84.2% patients were multipara and only 6.6% were nullipara by Nidhi Singh and Hanslata Gehlot[49].

In present study, 66% of the patients were more than 18 years at marriage with the mean age of the patients was observed as 18.34 ± 1.624 (years). Similarly Nidhi Singh and

Hanslata Gehlot[49] in 2019 documented that most of the women in our study group had age at marriage between 17 to 19 years were 49.4%.

In our study, most of the women with abnormal cervical cytology, (86%) had lower socio economic status. This was in concordance with Gudrun Broberg et al., 2018[52] Women with low disposable family income (adjOR 2.06; 95% confidence interval (CI) 2.01± 2.11).

Present study, most of the women with abnormal cervical cytology, (96%) had no multiple sexual partners. In contrast, Multiple sexual partners (21) were noted in Dawit Wolday et al., 2018 study,

Most of the women with abnormal cervical cytology, 49 (98%) had no partners with multiple sexual partners. Similarly, Yu huang et al.,[47] documented that (89.1%) had no multiple sexual partners.

Most of the women with abnormal cervical cytology, 43 (86%) had no history of STI. In contrast cervical cytology was abnormal in 30% of the HIV-positive women in S. Prathima et al[45] in 2021 study.

Present study, (100%) had no history of previous HPV infection. About (68%) had no use of condoms. Similarly, Kevin P McKenzie et al., in 2011[66] documented that less regular condom use (24%, P=0.02).

Most of the women with abnormal cervical cytology, 32 (64%) had no use of IUCD. This was in concordance with Leonard Ogbonna Ajah et al., 2016[61] study reports (4.5%) and (1.3%) of participants using IUD had Cervical Intraepithelial Neoplasia (CIN) 1 and CIN 2.

Our study, (92%) had no use of OCP. Supportively, Hui Jun Chih et al.,[64] shows that The duration of oral contraceptive consumption among women with abnormal Papanicolaou (Pap) smear result indicating CIN was significantly shorter than those without abnormal Pap smear result (mean±SD, 5.6±5.2 years vs. 8.2±7.6 years; p=0.002).

Present study, 50 (100%) had no hormone replacement therapy. all of the women with abnormal cervical cytology, 50 (100%) had no HIV. In contrast, 3.7% of women reported being HIV infected in Jonah Musa et al., 2020[48].

In regards, (66%) had no diabetic mellitus. Supportively, Shu Chen et al.,[57] showed that diabetes was related to poorer overall survival (HR=1.59, 95% CI: 1.35–1.87, P<.001) and poorer recurrence-free survival (HR=1.98, 95% CI: 1.47–2.66, P<.001) in cervical cancer patients.

Our study, most of the women with abnormal cervical cytology, (66%) had no immune suppressive agents, (100%) had no smoking habits, (100%) had no auto immune disorder.

About (60%) had complaints. Supportively in Umarani MK, Gayathri MN and Madhu Kumar R[60] showed that, commonest complaint was irregular bleeding per vagina and leucorrhea.

Present study, (100%) had no HPV vaccination status. Jiayao Lei et al., 2020[46] states that 57.4% (95% CI, 50.9–63.7) among women unvaccinated.

Our study, (88%) had no history of cervical cancer screening by Pap smear, (98%) had no history of colposcopy screening and (100%) had no history of testing of HPV.

About (58%) had LSIL of Bethesda classification. This was in concordance with Dania Al-Jaroudi, Tasnim Z. Hussain[68] shows that epithelial cell abnormalities were further classified

as atypical squamous cells of undetermined significance (ASC-US) 42.8%, atypical squamous cells of high grade (ASC-H) 14.3%, low-grade squamous intraepithelial lesion (LSIL) 28.5%, and glandular cell abnormalities (AGS) 14.3%.

Our study shows that, about (20%) had postitive HPV testing. statistically significant association of HPV infection with Bethesda classification among women with abnormal cervical cytology with chi-square value of (χ^2=9.791, d.f=2) at $p<0.05$ level. Similarly, Essaada Belglaia et al.,[63] 2015 showed that grade of cytological abnormalities was highly associated with HR HPV genotypes ($p = 0.001$ for LGSIL and $p < 0.0001$ for HGSIL).

This study shows that many woman came for cervical cancer screening only when symptomatic and not done regularly as guidelines suggests. Thus proving that cervical cancer screening awareness is poor thereby necessiating outreach programs to increase the awareness. And also HPV screening has been recommended in 2012 itself. Yet most of the gynecologist are preferring cytology alone which is less sensitive and have many interobserver interpretations rather than cotesting with HPV. Cotesting with HPV can extend the screening interval form 3 years to 5 years in screening schedule which most are unaware. Co testing also decreases unnecessary coloposcopic referral in patients with LSIL. When done cytology alone 29 of our patients with LSIL would have been referred to colposcopy for further mangement. Whereas in our study due to conjunction with HPV co testing, only 2 of the patients with LSIL and HPV positivity were referred for colposcopy for further management and others were advised for repeat cytology after a year. Our study also implies significance of HPV vaccination in routine immunisation as per IAP vaccination schedule.

CONCLUSION AND SUMMARY

CONCLUSION

- Cervical cytology is an essential tool for early detection of premalignant and malignant lesions of cervix.
- Invasive cervical cancer is appraised as a preventable disease due to its long pre-invasive state.Therefore, screening for premalignant cervical lesions represents an opportunity to prevent women progressing cervical carcinoma.
- HPV primary screening or cotesting with pap smear testing is necessary
- Cotesting with HPV can extend the screening interval from 3 years(with cytology alone) to 5 years
- Cotesting reduces colposcopic referral
- Importance of HPV vaccination in primary prevention of cervical cancer

SUMMARY

In the present study 50 patients who came to gynecology OP were included during the study period. Among the total 50 women with abnormal cervical cytology, 54% were in the age group ranging between 41-50 years with the mean age of the patients was observed as 44.14 ± 7.502 (years), 50% of patients had P2L2 Parity.

About 66% were more than 18 years at marriage with the mean age of the patients was observed as 18.34 ± 1.624 (years), (86%) had lower socio economic status, (96%) had no multiple sexual partners, (98%) had no partners with multiple sexual partners, (86%) had no history of STI. (92%) had no use of OCP, (66%) had no diabetic mellitus, (66%) had no immune suppressive agents, (60%) had complaints, (100%) had no HPV vaccination status, (88%) had no

history of cervical cancer screening by Pap smear, (98%) had no history of colposcopy screening and (100%) had no history of testing of HPV. About (58%) had LSIL of Bethesda classification.

Thus, demographic and behavioral characteristics related to Human Papilloma Virus infection in women with abnormal cervical cytology and supply an insight for the development of Human Papilloma Virus vaccines.

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PROFORMA

NAME	:
AGE	:
IP NO	:
ADDRESS	:
DATE OF SAMPLING	:
EDUCATION	:
SOCIOECONOMIC STATUS	:
AGE OF MARRIAGE	:
OBSTETRIC CODE	:
COMPLAINTS	:
LAST MENSTRUAL PERIOD	:
PAST HISTORY	
DIABETES	-
HYPERTENSION	-
HISTORY OF PREVIOUS STI	-
HISTORY OF PREVIOUS HPV INFECTION	-
SMOKING	-
OTHER IMMUNO DEFICIENCY STATE	-
FAMILY HISTORY	:
PARTNER WITH HPV	-
PARTNER WITH STI	-
MULTIPLE SEXUAL PARTNERS	-
OBSTETRIC HISTORY	:
HISOTRY OF OCP USE	-
HISOTY OF IUCD USE	-

HISOTRY OF CONDOM USE -

PREVIOUS HISTORY OF CERVICAL CANCER SCREENING -

GENERAL EXAMINATION :

HEIGHT :

WEIGHT :

PULSE RATE :

BLOOD PRESSURE :

CARDIOVASCULAR SYSTEM :

RESPIRATORY SYSTEM :

ABDOMINAL EXAMINATION :

VAGINAL EXAMINATION :

DIAGNOSIS :

PAP SMEAR	
HPV TESTING	

OTHER INVESTIGATION

Hb. Platelet count Hematocrit RBS Urea Creatinine

GOVT RAJAJI HOSPITAL, MADURAI MEDICAL COLLEGE-625020

INFORMED CONSENT

ASSOCIATION OF HPV INFECTION IN WOMEN WITH

ABNORMAL CERVICAL CYTOLOGY

நான் இந்த ஆராய்ச்சியில் விவரங்களை முற்றிலும் புரிந்து கொண்டேன் .

ஆய்வில் பங்கு எடுத்துபோது ,சாத்தியமான அபாயங்கள் மற்றும் பயன்களை பற்றி நான் அறிந்துள்ளேன் .

நான் எந்தவெருவேளையிலும் ஆய்வில் இருந்து திரும்ப முடியும் ,அதன்பின்னர் ,நான் வழக்கம் போல் மருந்துவ சிகிச்சை பெறமுடியும் என்று புரிந்து கொள்கிறேன்.

நான் ஆய்வில் பங்கு எடுத்து பணம் எதையும் பெற முடியாது என்று அறிந்துள்ளேன்.

இந்த ஆய்வின் முடிவுகள் எந்த மெடிக்கல் ஜர்னலில் வெளியிடப்பட இருந்தால் நான் எதிர்க்கவில்லை ,என் தனிப்பட்ட அடையாளத்தை வெளிப் படுத்தப்பட்டு இருக்க கூடாது .

நான் இந்த ஆய்வில் பங்கெடுப்பதன் மூலம் நான் என்ன செய்ய போகிறேன் என்று தெரியும் .

நான் இந்த ஆய்வில் என் முழு ஒத்துழைப்பையும் கொடுப்பேன் என்று உறுதியளிக்கிறேன் .

தன்னார்வளர் பெயர் மற்றும் முகவரி

கையெப்பம் / விரல்ரேகை

சாட்சி பெயர் மற்றும் முகவரி

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ஆரய்ச்சியாளராக

கையெப்பம் / விரல்ரேகை

INSTITUTIONAL ETHICS COMMITTEE
MADURAI MEDICAL COLLEGE & GOVT. RAJAJI HOSPITAL, MADURAI
CDSCO:Reg.No.ECR/1365/Inst/TN/2020 &
DHR Reg.No.EC/NEW/INST/2020/484

Study Title	:	Association of HPV infection in patients with Abnormal cervical cytology
Principal Investigator	:	**Dr.Ashwinilakshmi T.S**
Designation	:	PG in MS., Obstetrics & Gynecology
Guide	:	Dr.N.Sumathi, , MD.,DGO., Professor and HOD of Obstetrics & Gynaecology
Department	:	Department of Obstetrics & Gynaecology Government Rajaji Hospital & Madurai Medical College, Madurai

The request for an approval from the Institutional Ethics Committee (IEC) was considered on the IEC meeting held on **11.08.2021** at GRH Auditorium, Govt. Rajaji Hospital, Madurai at 10.00 A.M

The Members of the committee, the Secretary and the Chairman are pleased to inform you that your proposed project mentioned above is **Approved.**

You should inform the IEC in case of any changes in study procedure, methodology, sample size investigation, Investigator or guide or any other changes.

1. You should not deviate from the area of work for which you had applied for ethical clearance.

2. You should inform the IEC immediately, in case of any adverse events or serious adverse reactions. If encountered during from study.

3. You should abide to the rules and regulations of the institution(s)

4. You should complete the work within the specific period and if any extension is required, you should apply for the permission again for extension period.

5. You should submit the summary of the work to the ethical committee on completion of the study.

MEMBER SECRETARY,
IEC, Madurai Medical College,
Madurai
Dr.K.RAADHIKA, M.D(Pharm)
Associate Professor
Member Secretary
IEC - Madurai Medical College
Madurai.

16 AUG 2021

CHAIRMAN,
IEC, Madurai Medical College,
Madurai
Prof. Dr. V. Nagaraajan
MD.,MNAMS..DM..DSC(Neuro).,DSC(Hon)
CHAIRMAN
IEC Madurai Medical College
Madurai

PLAGIARISM CERTIFICATE

This is to certify that the dissertation work titled "**ASSOCIATION OF HPV INFECTION IN WOMEN WITH ABNORMAL CERVICAL CYTOLOGY IN GOVT RAJAJI HOSPITAL, MADURAI**" of the candidate **Dr ASHWINILAKSHMI.T.S,** with the registration number **221916103** for the award of **M.S Degree** in the branch of **Obstetrics and Gynaecology**. I personally verified the urkund.com website for the purpose of plagiarism Check. I found that the uploaded thesis file contains from introduction to conclusion pages and result shows **10 %** of plagiarism in the dissertation.

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S.NO	NAME	IP/OPNO	AGE	PARITY	AGEOF	SOCIOECONOMICSTAT	MULTIPL	PARTNE	HISTORY	HISTORY	USEOFC	USE OFI	USEOFO	HORMO	HIV	DIABETIC	IMMUN	SMOKIN	AUTOIM	COMPLAINTS	HPVVAC	HISTORY	HISTORY	HISTORY	BETHESD	HPVTEST
1	paralatchi	13452	30	P2L2	19	LOWER	NO	NO	YES	NO	YES	yes	NO	NO	NO	NO	NO	NO	NO	Screening	NO	NO	NO	NO	LSIL	NEGATIVE
2	pandiayammal	11567	60	P5L3	17	UPPERLOWER	NO	NO	NO	NO	NO	yes	NO	NO	NO	YES	YES	NO	NO	leucorrhoea	NO	NO	NO	NO	HSIL	POSITIVE
3	meena	12323	44	P2L2	16	LOWER	NO	NO	NO	NO	NO	no	NO	NO	NO	NO	NO	NO	NO	Screening	NO	YES	NO	NO	ASCUS	NEGATIVE
4	sarala	12456	42	P2L3	18	LOWER	NO	NO	NO	NO	NO	no	NO	NO	NO	NO	NO	NO	NO	leucorrohea	NO	NO	NO	NO	HSIL	NEGATIVE
5	kokila	12453	44	P1L2	21	LOWER	NO	NO	NO	NO	NO	no	YES	NO	NO	NO	NO	NO	NO	leucorrhoea	NO	NO	NO	NO	LSIL	NEGATIVE
6	valliyammal	12765	43	P2L2	17	LOWER	NO	NO	NO	NO	NO	yes	NO	NO	NO	NO	NO	NO	NO	Screening	NO	NO	NO	NO	LSIL	NEGATIVE
7	seetha	12875	55	P2L2A2	16	LOWER	NO	NO	NO	NO	NO	no	NO	NO	NO	NO	NO	NO	NO	Screening	NO	YES	NO	NO	ASCUS	NEGATIVE
8	ramya	12222	45	P2L2	18	LOWER	NO	NO	NO	NO	NO	yes	NO	NO	NO	YES	YES	NO	NO	leucorrhoea	NO	NO	NO	NO	LSIL	NEGATIVE
9	shenbagam	12348	56	P2L2	19	LOWER	NO	YES	NO	NO	NO	no	NO	NO	NO	YES	YES	NO	NO	Screening	NO	NO	NO	NO	ASCUS	POSITIVE
10	mariyammal	12643	53	P2L3	19	LOWER	NO	NO	NO	NO	NO	no	NO	NO	NO	NO	NO	NO	NO	leucorrhoea	NO	NO	NO	NO	LSIL	NEGATIVE
11	manimegalai	12532	32	P4L4	20	LOWER	NO	NO	NO	NO	YES	no	NO	NO	NO	NO	NO	NO	NO	Screening	NO	NO	NO	NO	LSIL	NEGATIVE
12	murugeshwari	12475	42	P2L2	21	LOWER	NO	NO	NO	NO	NO	no	YES	NO	NO	YES	YES	NO	NO	Screening	NO	NO	NO	NO	LSIL	NEGATIVE
13	reeta	13074	44	P4L2	22	LOWER	NO	NO	NO	NO	NO	no	NO	NO	NO	NO	NO	NO	NO	Screening	NO	NO	NO	NO	LSIL	NEGATIVE
14	sarala	13098	45	P2L2	18	LOWER	NO	NO	NO	NO	NO	no	NO	NO	NO	NO	NO	NO	NO	leucorrhoea	NO	NO	NO	NO	LSIL	NEGATIVE
15	latha	112631	44	P2L2	17	LOWER	NO	NO	NO	NO	NO	yes	NO	NO	NO	NO	NO	NO	NO	Screening	NO	NO	NO	NO	HSIL	NEGATIVE
16	sudha	12523	33	P2L2	18	LOWER	NO	NO	NO	NO	YES	no	NO	NO	NO	NO	NO	NO	NO	Screening	NO	NO	NO	NO	LSIL	NEGATIVE
17	pothumponnu	12756	53	P3L3	18	UPPERLOWER	NO	NO	NO	NO	NO	no	NO	NO	NO	NO	NO	NO	NO	Screening	NO	YES	NO	NO	LSIL	NEGATIVE
18	rukmani	12856	43	P2L2	19	UPPERLOWER	NO	NO	YES	NO	NO	no	NO	NO	NO	YES	YES	NO	NO	Screening	NO	NO	NO	NO	ASCUS	POSITIVE
19	vanmathy	12358	34	P3L3	17	LOWER	YES(IIM	NO	NO	NO	YES	no	NO	NO	NO	NO	NO	NO	NO	leucorrhoea	NO	NO	NO	NO	HSIL	NEGATIVE
20	manjula	12876	34	P4L3	17	LOWER	NO	NO	NO	NO	YES	no	NO	NO	NO	YES	YES	NO	NO	leucorrhoea	NO	NO	NO	NO	HSIL	NEGATIVE
21	muthumeena	12213	46	P6L3	15	LOWER	NO	NO	NO	NO	NO	no	NO	NO	NO	YES	YES	NO	NO	leucrrhoea	NO	NO	NO	NO	LSIL	NEGATIVE
22	kavitha	12436	45	P2L2A3	16	LOWER	YES(IIM	NO	NO	NO	NO	no	NO	NO	NO	YES	YES	NO	NO	Screening	NO	NO	NO	NO	LSIL	NEGATIVE
23	muthumari	12845	44	P2L2A1	18	LOWER	NO	NO	NO	NO	NO	yes	NO	NO	NO	YES	YES	NO	NO	leucorrhoea	NO	NO	NO	NO	LSIL	NEGATIVE
24	lakshmi	12999	46	P2L2	17	LOWER	NO	NO	NO	NO	NO	yes	NO	NO	NO	NO	NO	NO	NO	Screening	NO	NO	NO	NO	LSIL	POSITIVE
25	usha	12787	43	P2L2	18	UPPERLOWER	NO	NO	NO	NO	YES	yes	NO	NO	NO	NO	NO	NO	NO	leucorrhea	NO	NO	NO	NO	LSIL	NEGATIVE
26	priya	12690	44	P2L2A1	19	UPPERLOWER	NO	NO	NO	NO	NO	yes	NO	NO	NO	NO	NO	NO	NO	Screening	NO	NO	NO	NO	HSIL	NEGATIVE
27	alagumeena	12970	46	P2L2	20	LOWER	NO	NO	NO	NO	YES	yes	NO	NO	NO	NO	NO	NO	NO	leucorrhoea	NO	NO	NO	NO	ASCUS	POSITIVE
28	subha	18209	55	P2L2	21	LOWER	NO	NO	NO	NO	NO	yes	YES	NO	NO	YES	YES	NO	NO	Screening	NO	NO	NO	NO	LSIL	NEGATIVE
29	suganthi	10290	45	P2L3	20	LOWER	NO	NO	NO	NO	NO	no	NO	NO	NO	NO	NO	NO	NO	Screening	NO	YES	NO	NO	HSIL	POSITIVE
30	sasikala	11240	47	P2L2A2	21	LOWER	NO	NO	YES	NO	NO	no	NO	NO	NO	NO	NO	NO	NO	leucorrhoea	NO	NO	NO	NO	LSIL	NEGATIVE
31	kaarpagam	11979	46	P2L2	19	LOWER	NO	NO	NO	NO	NO	no	NO	NO	NO	NO	NO	NO	NO	Screening	NO	YES	NO	NO	HSIL	NEGATIVE
32	kamathi	10990	45	P2L2	18	LOWER	NO	NO	NO	NO	NO	yes	NO	NO	NO	YES	YES	NO	NO	Screening	NO	NO	YES	NO	HSIL	NEGATIVE
33	chithra	12910	54	P4L2	17	LOWER	NO	NO	YES	NO	NO	no	NO	NO	NO	NO	NO	NO	NO	Screening	NO	NO	NO	NO	ASCUS	NEGATIVE
34	vanitha	12989	50	P2L1A1	16	LOWER	NO	NO	NO	NO	NO	no	NO	NO	NO	NO	NO	NO	NO	Screening	NO	NO	NO	NO	ASCUS	POSITIVE
35	chandra	12937	40	P2L2	17	LOWER	NO	NO	NO	NO	YES	no	NO	NO	NO	NO	NO	NO	NO	leucorrhoea	NO	NO	NO	NO	LSIL	NEGATIVE
36	mythili	12222	43	P2L0	17	LOWER	NO	NO	NO	NO	NO	yes	NO	NO	NO	YES	YES	NO	NO	leucorrhoea	NO	NO	NO	NO	LSIL	NEGATIVE
37	thangam	12889	53	P2L2	18	UPPERLOWER	NO	NO	NO	NO	NO	yes	NO	NO	NO	YES	YES	NO	NO	leucrrhoea	NO	NO	NO	NO	HSIL	NEGATIVE
38	palaniyammal	12836	43	P1L1	19	UPPERLOWER	NO	NO	NO	NO	NO	no	NO	NO	NO	NO	NO	NO	NO	Screening	NO	NO	NO	NO	LSIL	NEGATIVE
39	dhanalakshmi	12768	43	P1L1	20	LOWER	NO	NO	NO	NO	YES	no	YES	NO	NO	YES	YES	NO	NO	leucorrhoea	NO	NO	NO	NO	LSIL	NEGATIVE
40	indhumahti	12987	55	P2L2	18	LOWER	NO	NO	YES	NO	NO	no	NO	NO	NO	NO	NO	NO	NO	Screening	NO	NO	NO	NO	LSIL	NEGATIVE
41	maheswari	12919	31	P2L2A1	17	LOWER	NO	NO	YES	NO	YES	no	NO	NO	NO	NO	NO	NO	NO	leucorrhea	NO	NO	NO	NO	HSIL	POSITIVE
42	jeyapriya	12768	35	P2L2	18	LOWER	NO	NO	NO	NO	YES	no	NO	NO	NO	NO	NO	NO	NO	Screening	NO	NO	NO	NO	LSIL	NEGATIVE
43	subbulakshmi	12786	35	P3L2	17	LOWER	NO	NO	NO	NO	YES	no	NO	NO	NO	NO	NO	NO	NO	leucorrhoea	NO	NO	NO	NO	LSIL	NEGATIVE
44	valliyammal	12864	34	P4L3	16	LOWER	NO	NO	NO	NO	YES	yes	NO	NO	NO	NO	NO	NO	NO	Screening	NO	NO	NO	NO	LSIL	NEGATIVE
45	sangeetha	12873	47	P2L2	21	LOWER	NO	NO	NO	NO	NO	yes	NO	NO	NO	YES	YES	NO	NO	Screening	NO	YES	NO	NO	LSIL	POSITIVE
46	hajira	12860	42	P2L2	20	LOWER	NO	NO	NO	NO	YES	yes	NO	NO	NO	YES	YES	NO	NO	leucorrhoea	NO	NO	NO	NO	HSIL	NEGATIVE
47	vidhya	12968	52	P4L2	19	LOWER	NO	NO	NO	NO	NO	no	NO	NO	NO	YES	YES	NO	NO	Screening	NO	NO	NO	NO	HSIL	NEGATIVE
48	shremathi	12869	56	PL2	19	LOWER	NO	NO	NO	NO	NO	no	NO	NO	NO	NO	NO	NO	NO	Screening	NO	NO	NO	NO	LSIL	NEGATIVE
49	sudha	12908	32	P2L2	20	LOWER	NO	NO	NO	NO	YES	no	NO	NO	NO	NO	NO	NO	NO	Screening	NO	NO	NO	NO	LSIL	NEGATIVE
50	akila	12889	34	P2L2	19	LOWER	NO	NO	YES	NO	YES	yes	NO	NO	NO	NO	NO	NO	NO	Screening	NO	NO	NO	NO	HSIL	POSITIVE