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CERVICAL CANCER: AN OVERVIEW

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Abstract - Cervical cancer stands as a formidable challenge in global healthcare, affecting women worldwide with significant morbidity and mortality rates. This review article aims to provide a comprehensive overview of cervical cancer, covering its introduction ,epidemiology, types, virology oh HPV, risk factors, preventions strategies, screening, and treatment and efforts made by WHO and Govt. of india .Cervical cancer is primarily caused by persistent infection with high-risk human papillomavirus (HPV) types, notably HPV-16 and HPV-18.Epidemiologically, cervical cancer remains a significant public health concern, particularly in low- and middle-income countries where access to screening and healthcare services is limited. Several risk factors influence the development of cervical cancer, including early age at first sexual intercourse, multiple sexual partners, immunosuppression, smoking, and lack of HPV vaccination. Clinically, cervical cancer often presents with nonspecific symptoms in its early stages, leading to delayed diagnosis and advanced disease at presentation. Screening programs employing cytology-based Pap smears or HPV testing have significantly improved early detection rates. Emerging technologies such as liquid-based cytology. Treatment modalities for cervical cancer encompass a multidisciplinary approach, including surgery, radiotherapy, chemotherapy, and targeted therapy. The choice of treatment depends on the stage of disease, patient characteristics, and treatment goals. Preventive strategies for cervical cancer encompass primary prevention through HPV vaccination, secondary prevention through screening and early detection, and tertiary prevention through effective treatment and follow-up care.

Index Terms - Cervical cancer, HPV, cytology, pap smear, carcinoma, virology, oncology, hysterctomy , staging, conization, trachelectomy, liquid based cytology

I. INTRODUCTION

Cervical cancer proceeds to rank among the best gynaecologic cancers around the world. [7] Cervical cancer is a cancer emerging from the cervix. It is due to the irregular development of cells that have the capacity to spread to other parts of the body. [1] At the beginning organize, No side effects are seen. Afterward indications may incorporate irregular vaginal dying, pelvic torment or torment amid sexual intercut. Whereas dying after sex may not be genuine, it may moreover show the nearness of cervical cancer. [2]

About 90% of cervical cancer cases are squamous cell carcinomas, 10% are adenocarcinoma, and a little number are other sorts. Determination is regularly by cervical screening taken after by a biopsy. Restorative imaging is at that point done to decide whether or not the cancer has spread

The to begin with cause of cervical cancer is Human papillomavirus disease (HPV) causes more than 90% of cases most who have had HPV contaminations, HPV 16 and 18 strains are capable for about 50% of tall review cervical pre-cancers. The others components which incorporate for having cervical cancer is smoking, frail safe framework, birth control pills, having numerous sex accomplice and beginning sex in youthful age, hereditary components are too dependable for having cervical cancer[2]

HPV antibodies ensure against two to seven high-risk strains of this family of infections and may avoid up to 90% of cervical cancers [3] As a chance of cancer still exists, rules prescribe proceeding standard Pap tests [3]. Other strategies of avoidance incorporate having few or no sexual accomplices and the utilize of condoms. [4] Cervical cancer screening utilizing the Pap test or acidic corrosive can distinguish precancerous changes, which when treated, can anticipate the advancement of cancer. Treatment may comprise of a few combination surgery, chemotherapy, and radiation treatment. Five-year survival rates in the Joined together States are 68%. Results, be that as it may, depend exceptionally much on how early the cancer is detected.[2]

Cervical Cancer can be cured, since it has a long pre obtrusive period. Early conclusion and treatment of Cervical Cancer at ladies are pivotal for decreasing mortality rates. Luckily Cervical Cancer has a long premalignant period that gives an opportunity for screening and treating some time recently it turns to be obtrusive Cervical Cancer. Population-based screening with Pap spread or cytology is an critical auxiliary preventive degree for Cervical Cancer that leads to a high-cure rate among Cervical Cancer patients. Early discovery and treatment by mean of screening can anticipate up to 80% of Cervical Cancers in created nations, where productive screening programs are input. In creating nations, be that as it may, there is constrained get to viable, wide scale screening, driving to expanded passings due to Cervical Cancer. [6]

Despite adequate prove supporting the utilize of screening as an viable mediation, there are still few large-scale screening programs being actualized in India. Information around malady and early screening is the most successful degree for Cervical Cancer avoidance. Need of

mindfulness, negative state of mind, and destitute hone almost Cervical Cancer and screening and preventive strategies are the major causes to increment the frequency of disease.[7]

In show disdain toward of a committed cancer control program in put in India, screening has not been successful to diminish the burden of illness. The thinks about appear that ladies have problematic level of information of Cervical Cancer, their state of mind is too favourable in any case the take-up of real hone is moo due to social shame. Due to shortage of writing with respect to information, state of mind, and hone (KAP) toward Cervical Cancer and its screening among Indian ladies this audit was conducted. The result of this think about gives data with respect to current mindfulness, demeanour and hone almost Cervical Cancer and screening, which is accommodating for planning population-based instructive program driving to information improvement approximately Cervical Cancer and its screening [7]

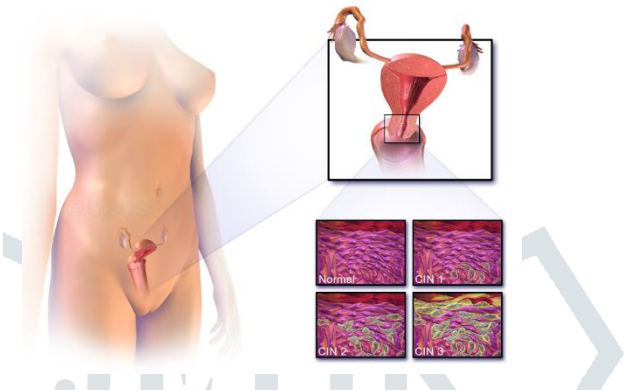

Figure no: 1 Showing cervical cancer stages

II. EPIDEMIOLOGY OF CERVICAL CANCER

Cervical cancer is one of the driving causes of cancer passing among ladies. Over the past 30 a long time, the expanding extent of youthful ladies influenced by cervical cancer has extended from 10% to 40 %. WHO and Worldwide Organization for Inquire about on Cancer (IARC) reports says that assessed, the year 2008 saw 529,000 unused cases of cervical cancer all inclusive. In creating nations, the cases of cervical cancer was 452,000 and positioned moment in malignancies in female patients. Then again, the number of modern cases of cervical cancer was 77,000 in created nations [5] Across the globe, 570 000 cases of Cervical Cancer and 311000 passings from the illness happened in 2018. Cervical [5] Cancer is the fourth most common cancer in ladies, positioning after breast cancer (2.1 million cases), colorectal cancer (0.8 million) and lung cancer (0.7 million) [6] According to the Reports HPV contamination causes more than 99% of all cervical cancers. Each year, there are more than 500,000 modern cases of cervical cancer and roughly 250,000 passings due to cervical cancer over the globe. Eighty percent of cases happen in creating nations. In the US, approximately 4000 ladies pass on annually from cervical cancer. Mortality is higher among ladies not screened in the past 5 a long time in created nations [7] 68%-84% of ladies are being screening by Pap spread, but in India this extent is 2.6%-5% as it were. This is one of the primary reasons that in India patients are being analysed at progressed or final stages.[6] It is the 2nd most driving cause of female cancer among ladies matured 15-44 a long time in India. Approximately 96, 922 modern Cervical Cancer cases are analysed yearly in India (in 2018). The components which are capable for improvement of Cervical Cancer is disease of human papilloma infection (HPV) sorts (HPV 16 and HPV 18), In China, cervical cancer is the moment biggest female threatening tumour. Concurring to the information from National Cancer Centre in 2015, there were 98,900 unused cases and 30,500 passings of cervical cancer. In the past 20 a long time, the rate and mortality of cervical cancer have been expanding steadily in China [5] In World, cervical cancer is the fourth-most common sort of cancer and the fourth-most common cause of passing from cancer in women.[5] In 2012, an assessed 528,000 cases of cervical cancer happened, with 2,66,000 passings. This is approximately 8% of the add up to passings from cancer. Approximately 70% of cervical cancers and 90% of passings happen in creating nations. In low-income nations, it is one of the most common causes of cancer passing with an rate of 47.3 per 100,000 ladies. In created nation.[26] Cervical cancer positions moment in rate and mortality behind breast cancer in lower Human Advancement File (HDI) settings; be that as it may, it is the most commonly analysed cancer in 28 nations and the driving cause of cancer passing in 42 nations, the tremendous lion's share of which are in Sub-Saharan Africa and South Eastern Asia. The most noteworthy territorial frequency and mortality rates are seen in Africa. In relative terms, the rates are 7–10 times lower in North America, Australia/New Zealand, and Western Asia (Saudi Arabia and Iraq) [5]

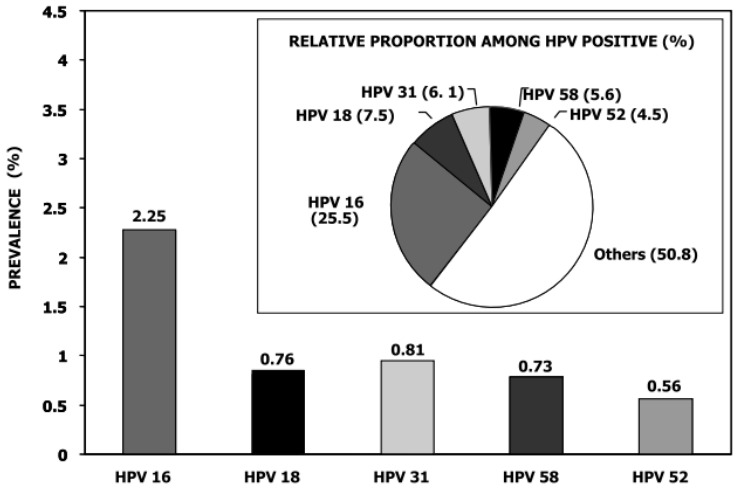

Figure no – 2 Overall HPV type specific prevalence & relative proportion of the 5 most common types among HPV positive women with normal cytology. [10]

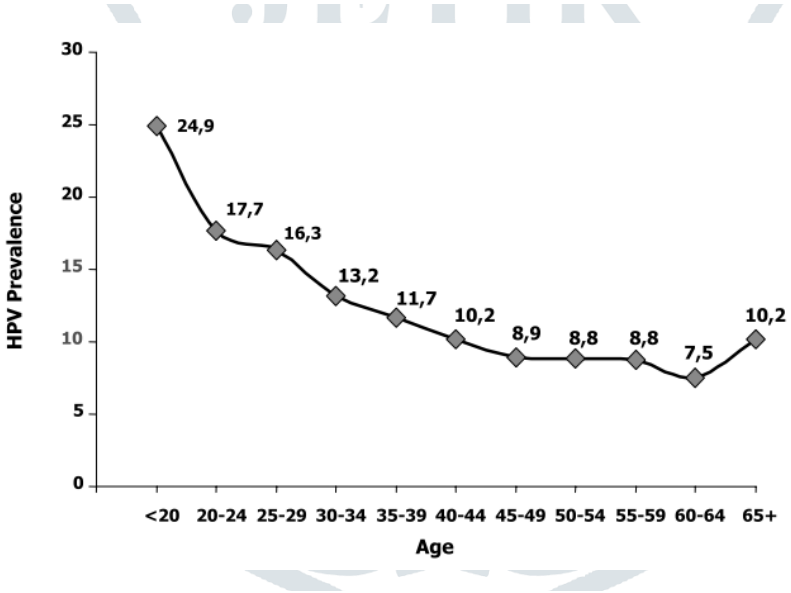

Figure No – 3 - World-wide age-specific HPV-DNA prevalence among women from the general population [10]

III. VIROLOGY OF HPV VIRUS

HPV belongs to the Papovaviridae family and is a relatively small, non-enveloped virus measuring around 55 nm in diameter. Its capsid is icosahedral, composed of 72 capsomers, each containing at least two capsid proteins: L1 and L2. L1 forms pentamers, while each virion capsid typically contains about 12 copies of the minor capsid protein, L2. The HPV genome comprises a single molecule of double-stranded, circular DNA, with all protein-coding sequences (Open Reading Frames or ORFs) located on one strand.

The genome contains three main functional regions: the "non-coding upstream regulatory region," also known as the long control region (LCR) or upper regulatory region (URR). This region exhibits the highest variability in the viral genome and includes the p97 core promoter, along with enhancer and silencer sequences regulating ORF transcription and DNA replication. The second region is the "early region (E)," which includes ORFs E1, E2, E4, E5, E6, and E7, involved in viral replication and tumorigenesis. The third region, known as the "late region (L)," encodes the L1 and L2 ORFs responsible for the viral capsid formation. For a new or unknown HPV type, the E6, E7, and L1 ORFs should exhibit less than 90% homology to the corresponding sequences of known HPV types. [8]

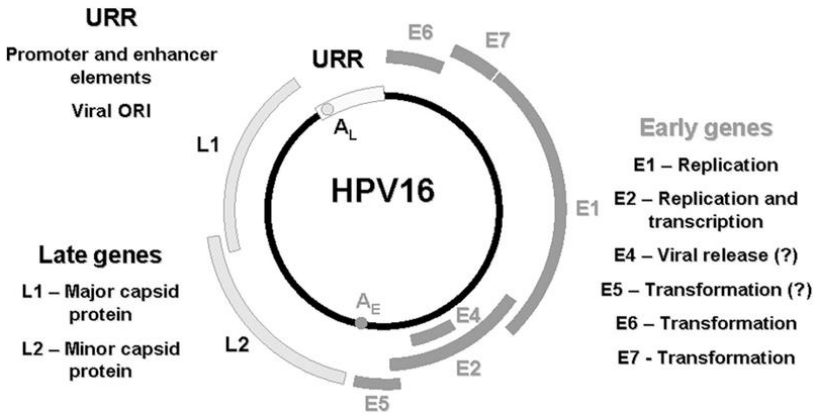

Figure no – 4 – Genomic Arrangement of HPV – 16 [8]

IV.TYPES OF CERVICAL CANCER

There are two types of Cervical Cancer

4.1. Squamous Cell Carcinoma

4.2. Adenocarcinoma

4.1 SQUAMOUS CELL CARCINOMA: Squamous Cell Carcinoma originates from the flat cells lining the cervix's bottom and is the most common type of cervical cancer, constituting approximately 90% of cases. It is identified by various characteristics including the degree of differentiation (ranging from well-differentiated to poorly differentiated), cellular features such as cytoplasmic appearance and nucleus size, presence of mitosis, and keratinization. The World Health Organization categorizes cervical epithelial tumours into different types of squamous cell carcinoma, each with distinct morphological and immunohistochemical features.

Assessment of Squamous Cell Carcinoma invasiveness involves examining features like stromal inflammation, desmoplastic reaction, dysplastic epithelial cell clusters, alterations in rete ridges, and loss of nuclear polarity. Histological differentiation is categorized as well, moderately, or poorly differentiated, with recent research indicating poorer outcomes in patients with poorly differentiated tumour. [11][12]

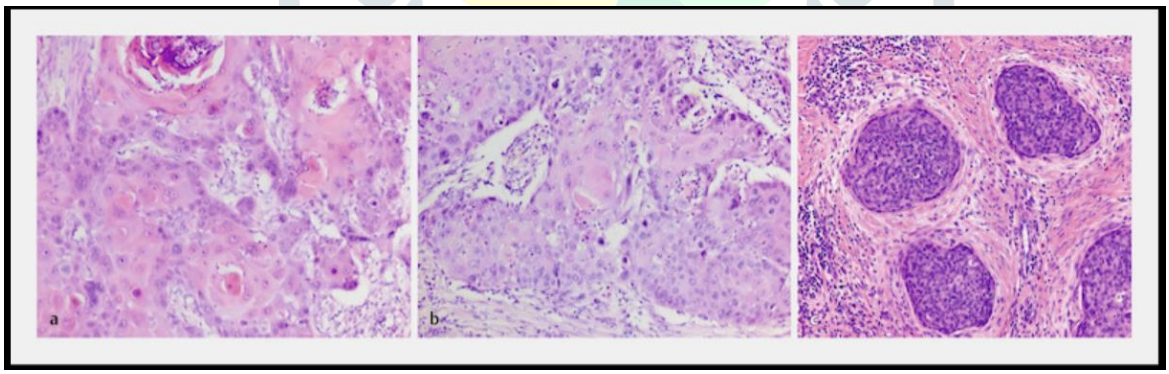

Figure no – 5 - Histology image of Squamous Cell Carcinoma

4.2. ADENOCARCINOMA: Adenocarcinomas of the cervix originate from the glandular cells found in the upper part of the cervix and represent the majority of remaining cervical cancer cases. These malignancies stem from epithelial cells in glandular structures and can occur in various locations throughout the body, including the breast, lung, prostate, and gastrointestinal tract. In fact, adenocarcinomas account for approximately 70% of cancers with unknown primary origin. Diagnosis of adenocarcinoma relies on identifying glandular structures through light microscopy, making it challenging to determine the tumour primary site, especially in cases of metastasis. Immunohistochemistry (IHC) becomes crucial in diagnosing poorly differentiated adenocarcinomas or those lacking visible glandular formation but staining positive for mucin. [13][14]

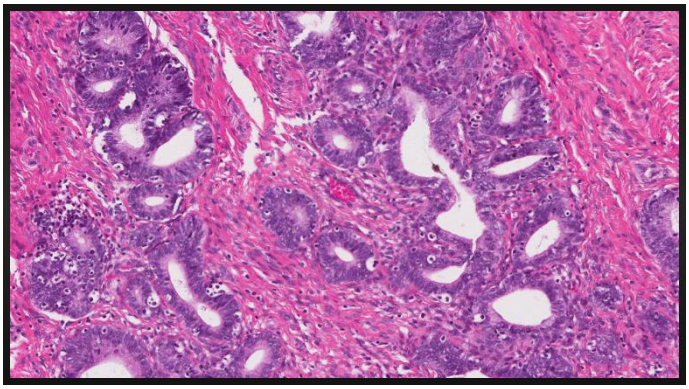

Figure no – 6 Histology of the adenocarcinoma

V. RISK FACTOR FOR CERVICAL CANCER

A few chance variables for cervical cancer are related with introduction to HPV.[5][27] The movement from forerunner injuries caused by sexually transmitted HPV to obtrusive cancer can amplify up to 20 a long time. [5] Additionally, different other components such as regenerative and sexual behaviours, smoking, early onset of sexual movement (some time recently age 16), having different sexual accomplices, tall equality, and lower financial status are too connected to an expanded chance of cervical cancer.[5][28]

5.1 SEXUALLUY TRANSMITTED DISEASES (STI)

5.1.1 HPV [Human papilloma infection]: The fundamental reason behind the improvement of precancerous and cancerous cervical injuries is the contamination with high-risk or oncogenic sorts of HPV. HPV16 and 18 are especially critical in causing cervical cancer. These high-risk sorts, particularly HPV16, are far reaching among human populaces. Transmission ordinarily happens through sexual contact, driving to squamous intraepithelial injuries. Whereas most of these injuries resolve inside 6 to 12 months due to safe reactions, a little division hold on and can advance to cancer. Research from meta-analyses demonstrates that the most elevated predominance of HPV contaminations is seen around the age of 25, conceivably related with shifts in sexual behaviours. A few districts display a bimodal dispersion of cervical cancer cases, where there is an introductory crest in the blink of an eye after the onset of sexual movement, taken after by a level amid adulthood. The moment crest in cases ordinarily happens after the age of 45.[5]

5.1.2 HUMAN IMMUNODEFICIENCY INFECTION (HIV): Ladies living with HIV have an hoisted hazard of contracting contaminations from high-risk HPV sorts. Investigate discoveries on the affiliation between HIV and cervical cancer demonstrate a higher predominance of tireless HPV diseases with different oncogenic strains, expanded anomalies in Pap smears, and a more prominent frequency of cervical intraepithelial neoplasia (CIN) and intrusive cervical carcinoma among HIV-positive people. HIV-infected ladies are more vulnerable to HPV disease at an prior age (13-18 a long time) and confront a increased hazard of creating cervical cancer. In comparison to non-infected ladies, HIV-positive patients with cervical cancer tend to be analysed at a more youthful age (15-49) a long time old).[5]

5.2 REPRODUCTIVE AND SEXUAL FACTOR

5.2.1 SEXUAL ACCOMPLICES: Variables relating to sexual behaviour have too been connected to cervical cancer. One think about found that an expanded hazard of cervical cancer is watched in individuals with numerous sexual accomplices.[32] Moreover, numerous considers have moreover recommended that ladies with different sexual accomplices are at tall hazard for HPV securing and cervical cancer .[33] From the meta-analysis, a noteworthy expanded chance of cervical illnesses was watched in people with numerous sexual accomplices compared to people with few accomplices, both in non-malignant cervical infection and in cervical cancer . The affiliation remained exist indeed after controlling for the status of HPV contamination, which is a major cause of cervical cancer. Moreover, early age at to begin with intercut is a hazard calculate for cervical cancer. [5]

5.2.2 ORAL CONTRACEPTIVE (OC) pills: Verbal prophylactic (OC) pills have been distinguished as a hazard figure for cervical cancer. Investigate from an universal collaborative epidemiological consider uncovered that the relative hazard of cervical cancer in current OC clients rises with drawn out term of utilize. Reports demonstrate that utilizing OCs for 5 a long time or more may twofold the hazard of cancer. Besides, in a multi- centre case-control think about including ladies testing positive for HPV DNA, the hazard of cervical cancer was found to triple among those who had utilized OC pills for 5 a long time or longer. A later precise audit and meta-analysis moreover highlighted a positive affiliation between OC pill utilize and cervical cancer hazard, especially for adenocarcinoma. This consider concluded that OC pill utilization freely contributes to the chance of creating cervical cancer. [34]

5.3 HAVING A DEBILIATED RESISTANT FRAMEWORK:

Having a compromised safe framework can reduce the body's capacity to combat HPV diseases. In people with debilitated insusceptibility, HPV diseases are more inclined to endure and development to cancer compared to those with a sound resistant framework. Components that may show immunocompromise include:

- Having HIV or another condition that compromises the safe system

- Taking medicines to smother resistant reactions, such as those utilized to anticipate organ dismissal post-transplant, oversee immune system infections, or treat cancer.[29]

VI. PREVENTION

As per the United States Preventative Services Task Force (USPSTF), cervical cancer screening typically begins at age 21 with Pap smear tests. At age 30, HPV testing is added to Pap smear cytology, and screening intervals are generally every 3 years for low-risk women with consistently negative results. For women over 30, screening intervals may extend to every 5 years when combined with HPV testing. A Level A recommendation suggests that low-risk women with consistently negative results can discontinue screening at age 65. Women who have undergone total abdominal hysterectomy for benign conditions do not require further screening.

Colposcopy is employed to evaluate abnormal cytology or detect high-risk HPV infections. The American Society for Colposcopy and Cervical Pathology (ASCCP) provides standard guidance for this procedure. Multiple colposcopic-guided biopsies and endocervical sampling are typically performed, except during pregnancy. Abnormal colposcopic findings may include acetowhite colour change, vascular abnormalities, mosaicism, and punctation.

Patients diagnosed with invasive disease undergo comprehensive staging using the International Federation of Gynaecology and Obstetrics (FIGO) staging system. This involves various methods such as pelvic examination, imaging (MRI and PET scans), and lab tests to assess the extent of the tumour. MRI is particularly useful for detecting local tumour extension, while PET scans are more sensitive for detecting nodal and visceral metastases, which are crucial for determining prognosis. [7]

The WHO's stance on HPV vaccination emphasizes its cost-effectiveness, especially in regions with limited resources. In India, HPV vaccines have been approved for females aged 9 to 45 years since 2008, endorsed by both the National Technical Advisory Group on Immunization (NTAGI) and the Indian Academy of Paediatrics Committee on Immunisation (IAPCOI) for girls starting at 9 years of age. FOGSI recommends vaccination between ages 9–14 as optimal, although older cohorts may still benefit. While vaccination might be less effective in sexually active females, it could still offer protection against previously unexposed HPV types.

A significant Indian study comparing the immunogenicity of two versus three doses of HPV vaccine found both regimens to be equally effective. Interestingly, even single-dose recipients exhibited a strong and lasting immune response, though not as robust as those who received two or three doses. Antibody levels remained stable over four years. Ongoing trials are exploring the feasibility of a single-dose vaccine. [35][36]

VII. SCREENING

Screening strategies for cervical cancer incorporate conventional Pap spread, visual assessment with acidic corrosive & Lugol's iodine (VIA/VILI), liquid-based cytology (LBC), and HPV testing. The presentation of Pap spread screening in created countries, outstandingly in the Joined together States since the 1950s, has contributed to a decrease in cervical cancer burden. In any case, the precision of conventional Pap spread can be influenced by different variables such as the quality of the cytological room, skill of professionals, inspecting procedures, slide quality, recolouring capability, and involvement of cytological personnel. In created nations with progressed research facility conditions and specialized mastery, the affectability of cytology ranges from 80% to 90%, whereas in resource-limited settings, it can drop to 30% to 40%. To address the confinements of conventional Pap spread screening, liquid-based cytology (LBC) was created and FDA-approved in 1996 for clinical utilize. LBC altogether progresses affectability and precision compared to conventional Pap spread strategies. In addition, organized and down to earth LBC screening programs have been executed in created nations, guaranteeing persistent and compelling cervical cancer screening strategies.[5]

CERVICAL CANCER SCREENING TEST

Cervical screening tests such as routine cytology (PAP spread), fluid based cytology (LBC), human papillomavirus (HPV) testing, and visual review on acidic corrosive (Through) can distinguish cervical precancerous injuries in clearly solid, asymptomatic ladies.[16]

7.1 CYTOLOGY: Cytology the think about of cells most broadly utilized methods in created or tall wage countries have screening offices coordinates with restorative and open wellbeing care administrations and have accomplished tall scope through superior program organization. This has brought about in considerable decays in cervical cancer rate and mortality over time.[16][17] A few of the creating nations in South and Central America and in Asia too actualized population-based cervical cancer screening utilizing cytology for a few decades. Be that as it may, these programs were generally incapable in lessening cervical cancer burden due to destitute scope with screening, treatment and follow-up care and need of quality assurance.[24] Larger part of the moo centrre pay nations (LMICs) have not one or the other started nor have the capacity to start and maintain quality guaranteed cytology screening programs in their immature and divided wellbeing administrations. In this Screening a smear are arranged by spreading the cervical cells test collected utilizing a spatula and cervical brush on a glass slide which is at that point settled and recoloured utilizing Papanicolaou (PAP) recolouring. Cytology is a profoundly subjective and supplier subordinate test with shifting execution between research facilities and cytologists perusing the smears.[16]

7.2 LBC {Fluid based Cytology}: Liquid-based cytology (LBC), a later progression in cervical cytology, revolutionizes example collection by lessening the event of unsuitable smears, minimizing flotsam and jetsam, and assisting translation time compared to conventional cytology. It marks the to begin with critical specialized movement in cervical cytology in over half a century. In LBC, cervical cell examples are flushed

into a fluid transport medium, sifted, and at that point a agent test is daintily spread on a slide to avoid cell cover. LBC tests can too be utilized for reflex HPV and other atomic testing, especially for triaging in cases of an ASCUS report. In any case, LBC illustrates comparative affectability and specificity to cytology in identifying CIN 2 or more regrettable lesions.[18]

7.3 HPV TESTING: HPV testing includes distinguishing HPV DNA or mRNA of two particular oncoproteins (E6 and E7) in cervical cell tests gotten through pelvic examination or self-sampling. It is recognized as the most exact, steady, and provider-agnostic strategy for cervical screening. Its capacity to identify CIN2+ injuries outperforms 90%, and CIN3+ injuries outperforms 95%, making it more delicate but less particular compared to cytology.[19] For ladies matured 30 and over, HPV testing is the favoured screening strategy since it permits for longer interims between screenings for those who test negative, regularly expanding up to 7-10 a long time due to the tall unwavering quality of a negative HPV test in foreseeing the nonattendance of CIN3 and cervical cancer [20]

7.4 VISUAL SCREENING TEST: By means of, or Visual Review with Acidic Corrosive, includes outwardly looking at the cervix with the exposed eye one diminutive after the application of a 3-5% weaken acidic corrosive arrangement beneath shinning light. Test comes about are categorized as negative, positive, or suggestive of intrusive cancer based on particular criteria.[21] A positive result is decided by the nearness of a particular, thick white zone adjoining to the squamocolumnar intersection (SCJ) in the change zone (TZ) of the cervix. This strategy is appropriate for screening premenopausal ladies beneath 50 a long time ancient, especially when the TZ is completely unmistakable on the ectocervix. In any case, translating the test comes about gets to be challenging in postmenopausal and more seasoned ladies. By means of is not suggested for ladies over 50 a long time of age or when the SCJ is not completely unmistakable. [16]

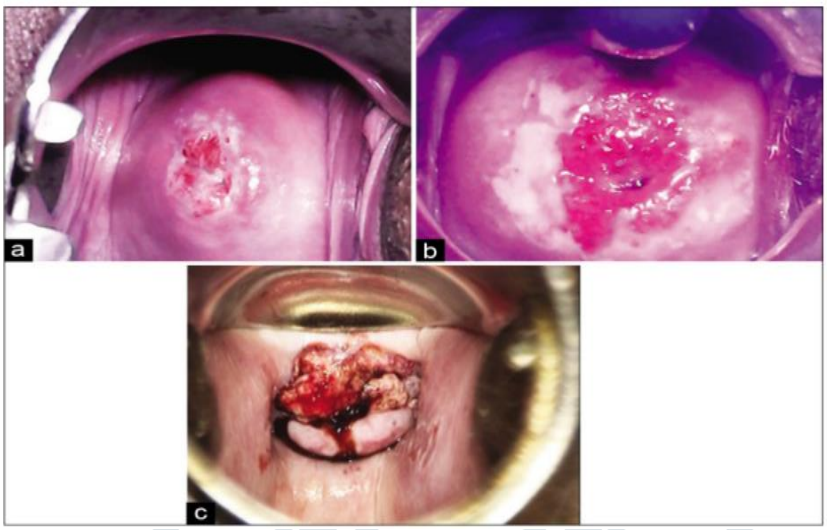

Figure no: 7 Visual inspection on acetic acid outcome categories. (a) VIA – Negative, (b) VIA – Positive, (c) VIA - Suspicious of invasive cancer.[16]

VIII. TREATMENT

Precancerous injuries are overseen conservatively for ladies more youthful than 25 a long time. Most positive discoveries in ladies more youthful than 25 a long time are low-risk cervical dysplasia and will resolve suddenly. Colposcopy assesses determined, irregular cytology or injuries suspected to be direct or tall hazard. These are overseen agreeing to findings. Low-risk injuries may be watched and reevaluated more regularly, and high-risk injuries are treated based on measure, profundity, and area. Cryotherapy or extraction is performed to oversee precancerous injuries constrained in estimate and profundity. Conization, laser, or circle electrosurgical extraction method (LEEP) are utilized to oversee injuries that incorporate the endocervical canal and are more broad. LEEP may give superior visualization of the squamocolumnar intersection and give the advantage of less dying in the outpatient setting. If obtrusive cancer is analysed, the another step in administration is arranging to decide assist treatment. Organizing is based on discoveries and comes about from detailed signs and side effects, examination, tissue pathology, and imaging. Evaluating is based on the estimate and profundity of the cancer and signs of spread to other organs. Treatment of early-stage malady is regularly surgical resection, extending from a conization to a altered radical hysterectomy. In any case, ladies with high-risk pathology postresection may require adjuvant treatment with chemotherapy and radiation. Conization or trachelectomy may be an alternative for ladies with early-stage illness who want future richness. For patients with more progressed malady, concurrent chemoradiation is the standard of care. [7]

Majorly there are four types of treatment for the cervical cancer

1 surgical Oncology

2 Radiation Oncology

3 Medical Oncology

4 staging

8.1 SURGICAL ONCOLOGY

Surgical removal is recommended for patients with early-stage cervical cancer limited to the cervix, with options ranging from less invasive procedures like cervical conization to more extensive ones like radical hysterectomy. While surgery is the preferred treatment for early-stage cases, it's particularly crucial for younger patients seeking to preserve ovarian function and/or fertility. Additionally, surgery is appropriate for certain patients with recurrent cancer.[7]

Types of Surgery

1 Cervical conization

2 Radical trachelectomy

3 Extrafascial hysterectomy

4 Radical hysterectomy

5 Pelvic exenteration

8.1.1 CERVICAL CONIZATION: Cervical conization is typically recommended for patients with carcinoma in situ (CIS) or stage IA1 invasive cervical cancer. This procedure involves using a scalpel or laser to remove the cervical transformation zone along with a portion of the cervix, ensuring a margin of at least 3 mm. It's crucial to thoroughly evaluate the margins and check for lympho vascular invasion (LVI) during pathological examination. In cases where a positive margin or LVI is detected, further excision or more extensive surgical intervention may be necessary. If there is no evidence of LVI in the specimen, the likelihood of lymph node involvement is extremely low, making nodal evaluation unnecessary. Patients with no adverse pathological findings may be placed under observation.[37]

8.1.2 RADIALTRACHELECTOMY: Patients who cannot undergo conization due to unfavourable pathological characteristics or advanced disease but still wish to preserve fertility may opt for a radical trachelectomy. This surgical procedure involves removing a significant portion of the cervix, excising the parametria, and mobilizing the ureters, bladder, and rectum. A small section (5 mm) of the cervix is preserved to accommodate the placement of a cerclage, which enables future pregnancy. Given the higher likelihood of lymph node involvement, a lymph node assessment such as sentinel node biopsy or pelvic lymphadenectomy is typically performed alongside radical trachelectomy. [38]

8.1.3 EXTRAFASCIAL HYSTERECTOMY : Extrafascial hysterectomy, also referred to as Type A radical hysterectomy, is reserved for a limited set of clinical situations. Generally, it is recommended for patients with stage IA1 cervical cancer who do not wish to preserve fertility. This surgical procedure entails the complete removal of the cervix and uterus. Optionally, ovarian removal may be considered, allowing for the preservation of ovarian function.[7]

8.1.4 RADIAL HYSTERECTOMY: A radical hysterectomy is presently considered for about all cases of early-stage cervical cancer where protecting ripeness is not a concern. The Querleu Morrow framework has supplanted the more seasoned Piver-Rutledge-Smith classification, rearranging the classification based on the degree of sidelong parametria resection. It portrays four sorts of radical hysterectomy (Sorts A through D). Sort A includes negligible parametrial resection, whereas Sort D involves total resection of the paracervical locale to the pelvic sidewall. The most commonly performed radical hysterectomies drop into Sorts B and C, which contrast in the degree of transection of the paracervical locale, either at the level of the ureters (Sort B) or the inner iliac vessels (Sort C).[39]

8.1.5 PELVIC EXENTERATION: Pelvic exenteration represents the most extreme surgical intervention for cervical cancer. It is typically recommended for patients with localized pelvic recurrence following radiotherapy or those with stage IVA disease who are not candidates for radiotherapy. A traditional total pelvic exenteration involves the removal of the uterus, fallopian tubes, ovaries, vagina, bladder, urethra, and rectum.[7]

8.2 RADIATION ONCOLOGY

Radiotherapy continues to play a vital role in the management of cervical cancer. Extensive randomized studies conducted during the 1990s and early 2000s have solidified the use of radiotherapy across various treatment modalities. It can be employed as primary treatment or as an adjunct therapy, either alone or in combination with platinum-based chemotherapy.

1 Early Stage cervical cancer

2 Advanced stage cervical cancer

8.2.1 EARLY STAGE CERVICAL CANCER: In cases of early-stage cervical cancer (stages IA1 to IIA1), radiotherapy can serve as the primary treatment approach. Combining external beam radiotherapy (EBRT) with a brachytherapy (BT) boost has shown to result in lower morbidity and comparable 5- and 20-year overall survival rates (83% and 75%, respectively) when compared to radical hysterectomy.[39] Some medical centres may opt for adjuvant hysterectomy in cases of bulky tumours following chemoradiation therapy, but this approach is generally not recommended by most guidelines due to notable complication rates. Recent data indicate that survival rates following chemoradiation therapy combined with adjuvant hysterectomy are less than optimal.[40]

8.2.2 ADVANCED STAGE CERVICAL CANCER: Locally aggressive and/or node-positive cervical cancer cases are commonly managed with definitive concurrent chemoradiotherapy, often incorporating platinum-based chemotherapy, followed by a brachytherapy boost. The integration of chemotherapy alongside definitive radiotherapy has demonstrated substantial enhancements in overall survival compared to radiotherapy alone, with an 8-year overall survival rate reaching 67% as opposed to 41%. Notable advancements in reducing both local recurrence rates and distant metastasis have also been observed as a result of this combined treatment approach.[7]

8.3 MEDICAL ONCOLOGY

8.3.1 DEFINITIVE THERAPY: The Radiation Therapy Oncology Group (RTOG) trials have established the effectiveness of platinum-based chemotherapy regimens in the treatment of cervical cancer. When compared to radiotherapy alone, these regimens consistently show benefits in overall survival, disease-free survival, and local control rates. It is theorized that chemotherapy functions as a radiosensitizer, enhancing the tumour response to radiation therapy. Among platinum-based agents, weekly cisplatin is the most commonly utilized. Single-agent platinum-based regimens have demonstrated superior progression-free survival and overall survival rates compared to non-platinum-based regimens. Additionally, they exhibit a more favourable toxicity profile in comparison to combinations of platinum-based regimens, such as cisplatin/5-FU/hydroxyurea.[41] In cases where patients cannot tolerate cisplatin, carboplatin may be used as an alternative.

8.3.2 ADJUVANT THERAPY: Some medical practices still opt for a combination of cisplatin and 5-FU, which is administered concurrently with radiotherapy. However, the choice of regimen may vary depending on individual patient factors and treatment goals.[42]

8.4 STAGING

The 2018 update to the International Federation of Gynaecology and Obstetrics (FIGO) staging system continues to be the primary methodology for staging. Although the American Joint Committee on Cancer (AJCC) Staging Manual's 8th edition also offers a tumour-node-metastasis classification system that aligns with FIGO stages, it is not commonly utilized in practice.

Traditionally, FIGO staging involved clinical assessment along with basic diagnostic procedures such as cystoscopy, proctoscopy, hysteroscopy, urography, and plain film x-ray. These methods were particularly valuable in resource-limited settings to accurately stage patients. However, modern advancements have introduced more sophisticated imaging modalities like MRI and PET scans into the staging process. Among these, MRI is preferred for determining tumour stage due to its superior tissue delineation compared to contrast-enhanced CT scans. [43]

Stage I: The condition is confined solely to the cervix, with the A/B distinction indicating the depth of invasion (≤5 or >5 mm).

Stage II: The ailment extends beyond the uterus but hasn't reached the lower vagina. This stage is further categorized as A/B depending on parametrial involvement.

Stage III: The illness has progressed to the lower one-third of the vagina (IIIA) or to the pelvic side wall and/or hydronephrosis (IIIB). Although traditionally nodal involvement didn't influence the FIGO staging, recent evidence shows it significantly impacts 5-year overall survival. [44] Consequently, new stages (IIIC1 and IIIC2) were introduced to signify pelvic or para-aortic (PA) nodal involvement.

Stage IVA: The disease displays local aggressiveness, affecting adjacent organs like the bladder or rectum.

Stage IVB: The ailment has spread to other distant solid organs; this stage may also indicate nonregional nodal disease.

IX. CERVICAL CANCER PREVENTIONS EFFORTS BY WHO AND INDIA

9.1 By World Health Organisation

In May 2018, the World Health Organization (WHO) called for the eradication of cervical cancer as a public health issue by promoting widespread HPV vaccination, screening, early detection, and treatment of cervical pre-cancer and cancer. On November 17, 2020, the World Health Assembly (WHA) officially launched a global strategy to implement this initiative. Despite the challenges posed by the COVID-19 pandemic, 194 countries pledged their support for this critical endeavour. The elimination program aims to reach the following objectives by 2030:

- Ensuring 90% of girls receive both doses of the HPV vaccine by the age of 15.

- Screening 70% of women using a high-performance test at the ages of 35 and 45.

- Ensuring 90% of women diagnosed with cervical pre-cancer and cancer receive treatment to reduce the incidence to less than four cases per 100,000 women.

Furthermore, the United Nations' Sustainable Development Goals for 2030 aspire to decrease premature mortality from non-communicable diseases by one-third through prevention and treatment. Achieving the targets set for cervical cancer elimination will contribute significantly to fulfilling this broader objective.[45]

9.2 National programmes for cancer control

In 1976 - The inception of the National Cancer Control Programme (NCCP) dates back to 1976, with its core aim being the promotion of cancer prevention through health education. Additionally, it focuses on secondary prevention by screening for cervical, oral, and breast cancers, enhancing the infrastructure of cancer treatment facilities, and offering palliative care to patients in the advanced stages of the disease.

In 2010 - In 2010, the NCCP merged with the NPDCS and was expanded to cover 21 states and 100 districts between 2010 and 2012. The initial phase review identified challenges, leading to program adjustments and expansion. Financial support for district-level activities is provided through the NHM. NCD clinics were established at district and community health centres to offer early diagnosis and treatment for common NCDs, with free diagnostic services and drugs provided. At a higher level, the TCCC scheme aims to enhance cancer care through the establishment of SCIs and TCCCs.

- At the primary level, ASHAs conduct door-to-door IEC activities and distribute educational materials. Medical officers monitor ASHA activities and provide regular training on screening. Mass screening campaigns and periodic camps are organized at subcentres, utilizing laboratory technicians and health workers for cytology/HPV screening at PHCs.

- At the secondary level, gynaecologists trained in colposcopy are available at CHCs, along with necessary equipment. Pathologists, chemotherapy, and palliative care services are provided. District-level monitoring and data management are conducted periodically.

- At the tertiary level, emphasis is placed on enhancing training at RCCs and institutes, particularly in surgical skills. Infrastructure for radiation and imaging techniques is improved. [45]

X. CONCLUSION

Cervical cancer remains a significant global health challenge, affecting women of all ages, races, and socioeconomic backgrounds. Despite advancements in medical science and technology, cervical cancer continues to claim the lives of thousands of women each year. Over the past few decades, concerted efforts in prevention, screening, treatment, and supportive care have led to notable progress in reducing the burden of cervical cancer. As we conclude this overview, it is imperative to reflect on both the achievements made and the challenges that lie ahead in the fight against cervical cancer. Primary prevention through vaccination against high-risk human papillomavirus (HPV) types stands as one of the most significant breakthroughs in cervical cancer prevention. HPV vaccination programs have been instrumental in reducing the incidence of HPV infection and associated cervical lesions, thus preventing the development of cervical cancer. Vaccination efforts have primarily targeted adolescents and young adults, aiming to confer immunity before exposure to HPV. In addition to vaccination, secondary prevention through cervical cancer screening plays a crucial role in early detection and treatment of pre-cancerous lesions, thereby reducing the incidence of invasive cervical cancer. Traditional screening methods, such as Pap smears, have been instrumental in detecting abnormal cervical cells and enabling timely intervention to prevent progression to cancer.. Combining HPV testing with cytology-based screening has further improved the accuracy and efficiency of cervical cancer screening programs, allowing for risk stratification and targeted follow-up based on individual risk profiles. Furthermore, advancements in screening technologies, such as liquid-based cytology offer promising opportunities to enhance the accuracy and efficiency of cervical cancer screening. Liquid-based cytology improves specimen adequacy and reduces the rate of unsatisfactory Pap smears, thereby minimizing the need for repeat testing and ensuring timely follow-up for abnormal results. In the realm of treatment, a multidisciplinary approach is essential for optimizing outcomes in patients diagnosed with cervical cancer. Treatment modalities for cervical cancer include surgery, radiotherapy, chemotherapy, and targeted therapy, with the choice of treatment depending on the stage of disease, tumour characteristics, and patient preferences. Surgical interventions, such as radical hysterectomy, are often employed for early-stage cervical cancer, aiming to achieve complete resection of the tumour while preserving fertility whenever possible. For locally advanced disease, concurrent chemoradiotherapy represents the standard of care, combining external beam radiation therapy with platinum-based chemotherapy to achieve optimal tumour control and improve survival outcomes. In cases of recurrent or metastatic disease, systemic therapies, including chemotherapy and targeted agents such as bevacizumab offer palliative benefits and may prolong survival in select patients. While treatment options for cervical cancer have advanced significantly in recent years, challenges such as treatment-related toxicity, treatment resistance, and access to specialized care remain significant barriers to optimal outcomes Comprehensive supportive care and survivorship programs are integral components of cervical cancer management, addressing the physical, psychosocial, and emotional needs of patients throughout their cancer journey. In conclusion, cervical cancer remains a significant global health challenge, but concerted efforts in prevention, screening, treatment, and supportive care have led to notable progress in reducing its burden. However, there is still much work to be done to achieve universal access to prevention and care services, eliminate disparities, and ultimately eradicate cervical cancer as a public health threat. By leveraging scientific advancements, fostering interdisciplinary collaboration, and prioritizing health equity, we can strive towards a future where cervical cancer is no longer a leading cause of morbidity and mortality among women worldwide.

XI. REFERENCES

1. National Cancer Institute. What is cancer? National Cancer Institute; National Institutes of Health. 2021
2. Cervical Cancer Treatment - NCI. (2022). Www.cancer.gov. https://www.cancer.gov/types/cervical/treatment#section/all
3. National Cancer Institute. Human Papillomavirus (HPV) Vaccines. National Cancer Institute; Cancer.gov.2021

4. Cervical Cancer Prevention (PDQ®) - NCI. (2024). Www.cancer.gov. https://www.cancer.gov/types/cervical/hp/cervical-prevention-pdq#section/all
5. Zhang S, Xu H, Zhang L, Qiao Y. 2020 .Cervical cancer: Epidemiology, Risk Factors and Screening. Chinese Journal of Cancer Research,32(6):720–728.
6. Taneja N, Chawla B, Awasthi A.A, Shrivastav K. D., Jaggi V. K., Janardhanan R.2021 Knowledge, Attitude, and Practice on Cervical Cancer and Screening Among Women in India: A Review. Cancer Control,28:107327482110107
7. Fowler J. R, Maani E. V, Dunton C. J, Gasalberti D. P, Jack B W. 2019Cervical Cancer. PubMed; StatPearls Publishing 2024
8. Okunade, K. S. 2019 Human papillomavirus and cervical cancer. Journal of Obstetrics and Gynaecology;40(5):602–608
9. World Health Organization. Cervical Cancer; World Health Organization;2023
10. Bosch F. X, de Sanjose S.2007 The Epidemiology of Human Papillomavirus Infection and Cervical Cancer. Disease Markers;23(4):213–227.
11. Jain M. A, Limaiem F.Cervical Squamous Cell Carcinoma. PubMed; StatPearls Publishing 2024
12. Brambs CE, Hohn AK, Hentschel B, Fischer U, Bilek K, Horn LC. 2019The Prognostic Impact of Grading in FIGO IB and IIB Squamous Cell Cervical Carcinomas. Geburtshilfe Frauenheilkd;79(2):198-204.
13. Greco FA, Lennington WJ, Spigel DR, Hainsworth JD.2015 Poorly differentiated neoplasms of unknown primary site: diagnostic usefulness of a molecular cancer classifier assay. Mol Diagn Ther;2:91-7
14. Jain M. A, Limaiem F.Cervical Squamous Cell Carcinoma. PubMed; StatPearls Publishing;2024
15. Remschmidt C, Kaufmann AM, Hagemann I,2013 Risk factors for cervical human papillomavirus infection and high-grade intraepithelial lesion in women aged 20 to 31 years in Germany. Int J Gynecol Cancer;23:519–26.
16. Banerjee D, Mittal S, Mandal R, Basu P.2005 Screening technologies for cervical cancer: Overview. Cytojournal2022;19,23.
17. Lyon France, Cervix Cancer Screening IARC; IARC Handbooks of Cancer Prevention;vol.10
18. Whitlock EP, Vesco KK, Eder M, Lin JS, Senger CA, Burda BU.2011 Liquid-based cytology and human papillomavirus testing to screen for cervical cancer: A systematic review for the U.S. preventive services task force. Ann Intern Med;**155**:687-97
19. Arbyn M, Ronco G, Anttila A, Meijer CJ, Poljak M, Ogilvie G, 2012Evidence regarding human papillomavirus testing in secondary prevention of cervical cancer. Vaccine;**30**(Suppl 5):F88–99
20. Sankaranarayanan R, Nene BM, Shastri SS, Jayant K, Muwonge R, Budukh AM. 2009HPV screening for cervical cancer in rural India. N Engl J Med,**360**:1385–94
21. Sankaranarayanan R, Wesley RS. A Practical Manual on Visual Screening for Cervical Neoplasia IARC Technical 2003 Publication No. 41
22. Sauvaget C, Fayette JM, Muwonge R, Wesley R, Sankaranarayanan R. 2011Accuracy of visual inspection with acetic acid for cervical cancer screening. Int J GynaecoObstet,**113**:14–24
23. Sankaranarayanan R, Nessa A, Esmy PO, Dangou JM.2012 Visual inspection methods for cervical cancer prevention. Best Pract Res Clin Obstet Gynaecol,**26**:221–32
24. Murillo R, Almonte M, Pereira A, Ferrer E, Gamboa OA, Jerónimo J, Lazcano-Ponce E.2008 Cervical cancer screening programs in Latin America and the Caribbean.Vaccine 26,(Suppl 11):L37–48
25. Safaeian M, Kiddugavu M, Gravitt PE, Ssekasanvu J, Murokora D, Sklar M, et al. 2007Comparability of self-collected vaginal swabs and physician-collected cervical swabs for detection of human papillomavirus infections in Rakai, Uganda. Sex Transm Dis,**34**:429–36
26. McGuire, S. (2016). World Cancer Report 2014. Geneva, Switzerland: World Health Organization, International Agency for Research on Cancer, WHO Press, 2015. Advances in Nutrition;7(2):418–419.
27. Cohen PA, Jhingran A, Oaknin A, 2019Cervical cancer. Lancet,393:169–82.
28. Roura E, Castellsague X, Pawlita M.2014Smoking as a major risk factor for cervical cancer and pre-cancer: results from the EPIC cohort. Int J Cancer,135:453–66
29. PDQ Cancer Information Summaries. Bethesda (MD): National Cancer Institute (US); 2002-Cervical Cancer Causes, Risk Factors, and Prevention: Patient Version ;2023.
30. Guimaraes Y. M., Godoy L. R., Longatto-Filho A., Reis R. dos. 2022Management of Early-Stage Cervical Cancer: A Literature Review Cancers,14(3):575.
31. Adler DH, Wallace M, Bennie T.2014Cervical dysplasia and high-risk human papillomavirus infections among HIV-infected and HIV-uninfected adolescent females in South Africa. Infect Dis Obstet Gynecol,498048
32. Cooper D, Hoffman M, Carrara H, 2007Determinants of sexual activity and its relation to cervical cancer risk among South African women. BMC Public Health,7:341
33. Remschmidt C, Kaufmann AM, Hagemann I, et al 2013Risk factors for cervical human papillomavirus infection and high-grade intraepithelial lesion in women aged 20 to 31 years in Germany. Int J Gynecol Cance,23:519–26.
34. Asthana S, Busa V, Labani S. 2020.Oral contraceptives use and risk of cervical cancer-A systematic review & meta-analysis. Eur J Obstet Gynecol Reprod Biol,247:163–75
35. Bhatla, N., Meena, J., Kumari, S., Banerjee, D., Singh, P., & Natarajan, J.2021.Cervical Cancer Prevention Efforts in India. Indian Journal of Gynecologic Oncology,19(3).
36. World Health Organization Human papillomavirus vaccines: WHO position paper, May 2017. Wkly Epidemiol Rec No,19(92):241–268
37. Larsson G, Gullberg B, Grundsell H.1983 A comparison of complications of laser and cold knife conization. Obstet Gynecol,62(2):213-7
38. Smith ES, Moon AS, O'Hanlon R, Leitao MM, Sonoda Y, Abu-Rustum NR, Mueller JJ. 2020Radical Trachelectomy for the Treatment of Early-Stage Cervical Cancer: A Systematic Review. Obstet Gynecol,136(3):533-542.
39. Landoni F, Maneo A, Colombo A, Placa F, Milani R, Perego P, Favini G, Ferri L, Mangioni C.1997 Randomised study of radical surgery versus radiotherapy for stage Ib-IIa cervical cancer. Lancet,350(9077):535-40

40. van Kol K, Ebisch R, Piek J, Beugeling M, Vergeldt T, Bekkers R. 2021Adjuvant Hysterectomy for Cervical Cancer Patients Treated with Chemoradiation Therapy: A Systematic Review on the Pathology-Proven Residual Disease Rate. Cancers (Basel),13(24)

41. Rose PG, Bundy BN, Watkins EB, Thigpen JT, Deppe G, Maiman MA, Clarke-Pearson DL, Insalaco S. 1999.Concurrent cisplatin-based radiotherapy and chemotherapy for locally advanced cervical cancer. N Engl J Med,340(15):1144-53
42. Peters WA, Liu PY, Barrett RJ, Stock RJ, Monk BJ, Berek JS, Souhami L, Grigsby P, Gordon W, Alberts DS. 2000.Concurrent chemotherapy and pelvic radiation therapy compared with pelvic radiation therapy alone as adjuvant therapy after radical surgery in high-risk early-stage cancer of the cervix. J Clin Oncol,(8):1606-13
43. Saleh M, Virarkar M, Javadi S, Elsherif SB, de Castro Faria S, Bhosale P. Cervical Cancer: 2018 Revised International Federation of Gynecology and Obstetrics 2020Staging System and the Role of Imaging. AJR Am J Roentgenol,214(5):1182-1195
44. Salib MY, Russell JHB, Stewart VR, Sudderuddin SA, Barwick TD, Rockall AG, Bharwani N.2020.FIGO Staging Classification for Cervical Cancer: Added Benefits of Imaging. Radiographics,40(6):1807-1822

45. Bhatla, N., Meena, J., Kumari, S., Banerjee, D., Singh P, Natarajan, J. (2021). Cervical Cancer Prevention Efforts in India. Indian Journal of Gynecologic Oncology,19(3).