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Cervical Cancer and its Probable Ayurvedic Approach

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ABSTRACT:

Cervical Cancer is the second most common cancer among women worldwide. Over 500,000 women worldwide die of cervical cancer annually. Human Papilloma Virus (HPV – mainly high risk type) is the main cause of cervical carcinogenesis. Worldwide, the prevalence of HPV in cervical tumors is 99.7% ¹. Approximately every 47 minutes a woman is diagnosed with cervical cancer. Among the 500,000 new cases each year, nearly 75% occur in developing countries ¹. Cervical cytological testing has reduced the incidence of cervical cancer by 70% ¹. As most of the cervical cancers are preventable so it become very important to diagnose them at an early treatable stage using appropriate diagnostic tools and finding new Ayurvedic measures to prevent and cure the disease so as to decrease the morbidity and mortality.

Key Words - Ayurvedic measures, Cervical cancer, Human papilloma virus, *Samprāpti*.

INTRODUCTION

Cervical cancer is a malignant tumor deriving from cells of the cervix. It develops quite slowly and begins with a precancerous condition known as dysplasia. Cervical cancer tends to occur where the two cell types meet (viz. squamous epithelium and glandular/columnar epithelium). The prevalence is more amongst the comparatively younger age group¹. HPV is the main cause of cervical cancer. HPV is an epitheliotropic virus which means it have tendency to attach with cervical epithelium. HPV infected cells are called Koilocytes (enlarged with

perinuclear halos). Nucleus is large, irregular, hyperchromatic. Over 99.7 percent of patients with CIN and invasive cancer are found to be positive with HPV DNA.² High risk HPV types include 16, 18, 31, 33, 35, 45, 56 types, out of which type 16 is responsible for more than 50% cases.³ Before the development of invasive carcinoma, there are different levels like CIN (Cervical Intraepithelial Neoplasia), CIS (Carcinoma In- situ) at which the disease can be prevented or cured, if detected earlier. So, it becomes important to use various Ayurvedic formulations and procedures which are told in classical



texts for other resembling health conditions. Various trials and studies are being done in this direction with benefit, helping in prevention and cure of cervical cancer, as mentioned in fore coming text.

AIM

To prevent cervical cancer with the help of various Ayurvedic measures mentioned under *Cikitsā* of *Vraṇa* and *Śotha*, like *Śodhana*, *Ropaṇa*, *Doṣa Śamana* and *Roga Apunarbhava* with the help of *Rasāyana Dravya Prayoga*.

OBJECTIVES

- (1) Formulating a possible *Samprāpti* of cervical cancer based on different *Nidāna* (causative factors) mentioned in texts.
- (2) To know about specific regimes like *Rajaswalācaryā* and various procedures mentioned in Ayurvedic texts like *Yoni Prakṣālana, Yoni Picu, Agnikarma* etc. which could be useful in prevention of cervical cancer.

METHODOLOGY

Various Ayurvedic classics, commentaries, modern literatures, research journals are used for the collection of literary references. Portals like PubMed central, Ayush research portal, Google scholar etc. are used as online sources of data collection.

Risk Factors⁴

- i. Women with high-risk HPV, HIV, Chlamydia infection. STDs.
- ii. Multiple sexual partners.
- iii. Early sexual intercourse.
- iv. Early age of first pregnancy.
- v. Too many or too frequent birth.
- vi. Low socioeconomic status.
- vii. Poor maintenance of local hygiene
- viii. Husband whose previous wife died of cervical carcinoma.
- ix. Oral pill users.
- x. Smoking habits.

Prevention

Primary Prevention⁵

- 1. Identifying the causal factors and eliminating or preventing them
- 2. Prophylactic HPV vaccine Approved to all school girls (12–18 years), women (16–25 years)
- 3. Use of condom during early intercourse
- 4. Raising the age of marriage and of first birth
- 5. Maintenance of local hygiene

- 6. Effective therapy of STIs
- 7. Removal of cervix during hysterectomy

Secondary prevention -

- 1. Involves identifying and treating the disease earlier in the more treatable stage.
- 2. This is done by screening procedures.

Cytologic Screening -

- Pap smear (Papanicolaou)
 - It is the gold standard for screening, however NICE (National Institute of Clinical Excellence) recommends to replace it with LBC (Liquid Based Cytology).⁶
- Ayre's spatula is used for squamocolumnar junction sampling and cytobrush is used for taking the endocervical sampling.
- The collected material is immediately spread over a microscopic slide and put into 95% ethyl alcohol for fixation.
- 3. After 30 min. fixation, it is air dried and then stained with Papanicolaou's or Sorr's method and examined by cytologist.

HPV Triage Strategy⁷ (**Fig. – 1.**)

Pathogenesis of HPV Infection -

- 1. HPV inserts itself into the immature squamous cells of the transformation zone (Fig. -2).
- 2. This virus integrates its DNA into host DNA.
- 3. Using the host DNA, HPV makes huge amounts of two of its proteins E₆ and E₇.
- 4. These proteins are responsible for pushing mature squamous cells through the cell replication cycle by blocking the action of tumor suppressor genes like p53.
- The end result is uncontrolled replication of cervical epithelial cells which are resistant to apoptosis or normal programmed cell death.

Dysplasia and Cancer Development

- 1. Normally, mature cells are stuck in G₁ or Growth 1 phase of cell cycle during which the cells grow and do important functions like protein synthesis and energy production.
- 2. Whenever new cells are needed, they will exit the G₁ phase and divide into two identical daughter cells.
- 3. But during this pathological condition, cells are pushed out of G_1 and go through the cell reproduction cycle faster than the body needs new cells.

- 4. This uncontrolled growth and multiplication is called dysplasia and it is exactly how cervical cancer develops from the precancerous cells.
- There is replacement of columnar epithelium at squamocolumnar junction either by the process of squamous epidermization or by metaplasia of reserve cells.
- 6. Under low vaginal pH, it results into the formation of immature unstable cells.
- 7. If the host immune defense is good, then these immature unstable cells undergo physiologic metaplasia and form well differentiated squamous epithelium.
- 8. But if there is presence of carcinogens, high risk type HPV infection, risk factors, poor immunity, then these immature unstable cells undergo Atypical metaplasia resulting in CIN and later on CIS and invasive carcinoma.

Types of Cervical Cancer

Gross Pathology (Based on Naked Eye Appearance)

- **Exophytic type** Arise from ectocervix, form friable masses, filling the upper vagina.
- Ulcerative type Here, lesion excavates the cervix and it often involves the fornices.
- **Infiltrative type** It is found as endocervical growth. It causes expansion of the cervix

making it barrel-shaped.

<u>Histopathology</u> (Depending upon the cells involved)

1. Squamous cell carcinoma (85-90%) (Fig 2)

Three groups: (i) large cell keratinizing

- (ii) large cell non-keratinising
- (iii) small cell type (Poor prognosis)

Arise from - Ectocervix.

Sources - Squamocolumnar junction

Squamous metaplasia of the columnar epithelium

2. Adenocarcinoma (10-15%)

Develops from - Endocervical canal [lining epithelium/glands]

More incidence in - younger age group

Adenoma-malignum - Extremely well-differentiated adenocarcinoma with favorable prognosis.⁸

Clinical Features of Cervical Carcinoma

- 1. **Irregular or continued vaginal bleeding** (may be brisk)
- 2. Offensive vaginal discharge
- 3. **Pelvic pain** (due to uterosacral ligament/sacral plexus involvement)
- 4. **Leg edema -** due to progressive obstruction of lymphatics and veins by the tumor.

5. **Bladder symptoms** - Frequency of micturition

- Dysuria
- Hematuria
- Incontinence due to fistula formation.

6. Rectal involvement - Diarrhea

- Constipation (late stages)
- Rectal pain
- Bleeding per rectum
- Rectovaginal fistula.
- Ureteral obstruction Pyelonephritis due to ureteric obstruction

Probable Ayurvedic Correlations of Cervical Cancer

1. Rakta Arbuda

As per Ācārya Suśruta, vitiated Doṣa compressing and constricting the blood and blood vessels, produces fast growing muscular protuberance, which may or may not suppurate, is associated with moist discharges and is covered with muscular sprouts.

There is continuous discharge of vitiated blood and the patient becomes

Pānduvarņa. Ācārya considered it incurable.9

2. Granthibhūta Ārtavadusti

 $\bar{A}c\bar{a}rya$ Suśruta mentioned $V\bar{a}ta$ and Kapha Doṣa responsible for this. Pelvic pain in cervical cancer could be due to $V\bar{a}ta$ and foul smelling discharges due to vitiation of Kapha Doṣa. The blood mixed discharges are clotted in appearance. It is kept under $As\bar{a}dhya$ category 10,11

3. Mutra-Purīṣa-Gandhi Ārtavadusti

There is presence of smell of urine and feces in menstrual blood. Such type of condition may occur in third and fourth stage of cervical carcinoma. It is also kept under *Asādhya* category. ¹²

4. Sannipātaja Asṛgdara

On the basis of foul smelling, multicolored discharges, severe anemic condition and incurability, it could be correlated with cervical cancer condition.¹³

5. Arista Ārtava Laksana

Under description of Arista Laksana (features of incurability) of $\bar{A}rtava$, $H\bar{a}r\bar{t}ta$ has mentioned that the woman suffering from fever, having very short intermenstrual period and continuous bleeding is incurable. ¹⁴

Pathya - Apathya

Ācārya Yogaratnākara mentioned the common Pathya and Apathya in Galagaṇḍa-granthi-arbudādi Cikitsā, which

could be beneficial in cervical cancer prevention.¹⁵

Pathya - Purāṇa Ghṛta Pānam, Jīrṇa Lohita Śāli (1 year old Lohita Śāli rice), Yava, Mudga, Paṭola, Raktashigru, Kaṭhillaka (Śāka of Boerhaavia diffusa), Śāli rice, Vetrāgra Śāka, Dravyas having Rukṣa, Kaṭu, Dīpana properties, Guggulu, Śilājīt etc. should be consumed.

Apathya - Excessive use of Sugarcane and Milk products, Māmsa of Aquatic animals, Piṣṭānna, Dravyas having Madhura, Amla Rasa in abundance, Guru and Abhiṣyandi properties should be avoided.

Possible Pathogenesis based on different *Nidānas* (Chart No. 1.)

Preventive Measures

A. Procedures

- 1. Rajaswalācaryā Eating Yava (Barley), milk, Śāli, Ghrta for 1st 3 days during menses. Ghrta increases the level of HDL, which is a plasma antioxidant. 16 Śāli rice have Tridosa Śāmaka and Brhmana properties. 17 Milk is Bṛhmaṇa and Rasāyana. Yava have Guru, Madhura, Śīta, Sara properties. During menses it is used Karśanārtha and Koşthaśodhanārtha. It is Agnivardhaka, Purīşajanaka. It also has mild Vātakara property which is pacified by adding milk in it. It is Kapha, Pitta, Rakta Vikārahara also. Vāta take out menstrual fluid out from the body and thus causing Śodhana. So, every woman should follow it to eliminate the *Doşas* from body. 18 If woman takes heavy food these days, then Vāta mix with Pitta Dosa and interferes with the food digestion resulting in Agnimāndya. As Rajaswalācaryā helps to maintain the hormonal balance, thus it helps in controlling the expression of Estrogen recptor $-\alpha$ which is responsible for the stimulation of reproductive tract proliferation.¹⁹
- **2. Yoni Prakṣālana** Ayurvedic vaginal douching performed with herbal remedies (eg. Triphalā Kwātha, Pancavalkala Kwātha). The procedure is highly recommended to all women suffering from recurring vaginal flora problems. It helps in maintaining the vaginal pH and helpful in prevention of cervical cell pathology.
- **3.** *Yonivarti Kṣāra Karma* by *Kasīsādi Kṣāra* in one sitting followed by *Dārvyādi Yoni Varti* of 3 gm once at bed time from next day for 21 days is found to be effective in the management of primitive cervical cell pathology, ²⁰ thus helpful in reversal of premalignant lesions like LGSIL. *Yonivarti* have *Vraṇaśodhana* property so it cleans the eroded area. It is *Kledahara* and *Krmighna*, thus

reduces the abnormal vaginal discharges and inhibits growth of microorganism. Then due its *Ropaṇa* and *Sandhānakara Karma*, is causes healing and rejuvenation.

- **4.** Agnikarma Śalāka made from Swarṇa have anticancer properties. Agnikarma is effective in treating cervical erosion, CIN I.²¹ As per Ācārya Suśruta Agnikarma have Vraṇa Śodhana, Vraṇa Ropaṇa, Sirā Sankocana, Chedana, Doṣa Śamana, Rogāṇam Apunarbhava properties.²² It is better than electric cauterization as it prevents the recurrence and excessive vaginal discharge.²³
- **5.** Virecana Karma Virecana have Srotośodhana and Vātānulomana properties. It also brings Budhi Śudhi and Prasādana, having a decompressing effect over the system. Due to the Vyavāyiguṇa of Virecana Dravyas they get circulated quickly into large and small blood vessels of the body. Due to Vikāsiguṇa, the Malas are detached from their respective Dhatus. By virtue of its Uṣṇa and Tīkṣṇaguṇas the accumulated Doṣas get liquefied and disintegrate into small particles at cellular level. Then these vitiated Doṣas and Malas are expelled out of the body through the Adhomārga.²⁴ By the Anulomana of Prāṇavāyu and Śodhana Karma it is helpful in pacifying the Doṣas and detoxifying the body from free radicles.
- **6.** *Yoni Picu* It could be done with *Jātyādi Taila, Tila Taila, Kṣāra Taila* etc. causing *Vraṇa Śodhana* and *Ropaṇa*. It is also beneficial in maintaining the vaginal pH.

B. Drugs and Formulations

- 1. Haridrā (Curcuma longa) It contains Curcumin which is a powerful antioxidant. It neutralizes the free radicals that increase the risk of cancer. It inhibits the growth of cancerous cells and reduces the chance of Radiation dermatitis after radiotherapy. Curcumin is cytotoxic to cervical cancer cells in a concentration-dependent and time-dependent manner. It selectively acts on HPV16 and HPV18 infected cells compared to non-HPV infected cells. Curcumin induces apoptosis in cervical cancer cells and selectively inhibits the expression of viral oncogenes E6 and E7.25 The administration of oral turmeric oil for a period of 12 weeks resulted in the arrest or regression of the premalignant condition, LGSIL, as detected by Pap smears during the therapy period. It was observed that the lesion in Pap smears was arrested in 3/19 cases and regressed in 16/19 cases.26
- 2. Āmalaki (Emblica officinalis) It exhibits its

anticancer activities through inhibition of AP-1 and targets transcription of viral oncogenes responsible for development and progression of cervical cancer thus indicating its possible utility for treatment of HPV-induced cervical cancers.²⁷

- **3. Ginger** (*Gingiber officinalis*) It contains *Gingerols* and *Zerumbone*. These particularly significant for cancers which show high levels of inflammation, which is a characteristic of cervical cancer.²⁸
- **4. Holy Basil** (*Occimum sanctum*) It contains Ursolic Acid which is very helpful in cancer.²⁹
- **5.** Aśwagandhā (Withania Somnifera) It contains Withferin A. Withaferin A induces p53-dependent apoptosis by repression of HPV oncogenes and upregulation of tumor suppressor protein in human cervical cancer cells. Thus, it shows tremendous cytotoxic activity and act as an anti-carcinogenic agent.³⁰
- **6.** *Basant* A clinical trial was carried out with the aim of elimination of HPV-16 in women with early Cervical Intraepithelial Lesions. The trial drug was "*Basant*", a polyherbal cream containing *Curcumin* from *Curcuma longa*, purified extracts of *Emblica officinalis*, *Azadirachta indica* leaves and *Aloe vera* (*Aloe barbadensis*). It was given for duration of 30 days and in result, overall, 80% clearance of HPV 16 was observed.³¹
- **7. Arsenic trioxide -** A study was carried out on patients with advanced cervical cancer. It showed that Arsenic trioxide induces apoptosis in HPV 16 DNA immortalized human cervical epithelial cells in vitro and selectively inhibits early viral gene expression.³²
- **8.** Anti-cervical cancer-cell properties of *Clerodendrum viscosum* root extract- *Clerodendrum viscosum* (CV) is a commonly growing weed in the Indian subcontinent has been employed by S. Nirmalananda (Ayurvedic expert) for the treatment of cervical cancer. They isolated and characterized a water extract fraction (Cv-AP) from the root of CV and evaluate its anticervical cancer cell bioactivity. Results showed that Cv-AP possesses pro apoptotic, anti-proliferative and anti-migratory activity in a dose-dependent fashion against cervical cancer cell lines.³³

DISCUSSION

Cervical cancer is highly preventable if detected earlier and proper measures are taken for its prevention and cure. Due to lack of awareness and due to various personal reasons, very small number of females undergoes regular screening procedure. There is also a lack of knowledge of various preventive measures for HPV (Human Papilloma Virus). Negligence and failure to treat the precancerous condition are the main causes behind the chronicity of the disease. All this result in its poor prognosis. The major part of population having low socioeconomic status suffer the most due to their illiteracy, lack of awareness regarding personal hygiene and screening procedures, hesitation in talking about such things. The patients avoid consulting a doctor until it becomes a major issue and creating so many problems like chronic menstrual irregularities, severe backache, pain abdomen, urinary dysfunctions etc. Also, HPV vaccinations have an important role in prevention of cervical cancer but very few are aware to this and very less number of women gets vaccinated. Different Ayurvedic procedures are very effective in prevention and complete cure of the disease if the measures are taken in early stages of dysplasia. So, it is the need of time to create awareness about the screening procedures, HPV vaccination and various Ayurvedic measures and medications should be used for the prevention of cervical cancer.

CONCLUSION

As much of occurrence of cervical cancers is due to HPV, the number of screenings should be increased more among the rural population. Further, the *Nidāna* responsible for the development of the disease should be avoided so as to break the *Samprāpti* chain. The specific regimes like *Rajaswalācaryā* should be followed and simple but effective procedures like *Yoni Prakṣālana* and *Picu* should be used for prevention. This will help to improve the quality of life in females and also in decreasing the morbidity and mortality from such a preventable disease.

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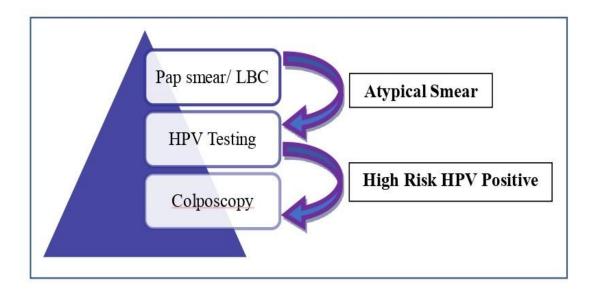


Fig. – 1. HPV Triage Strategy

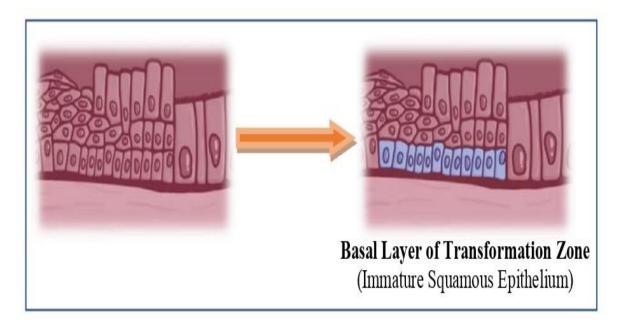


Fig. – 2. Immature squamous cells of the transformation zone

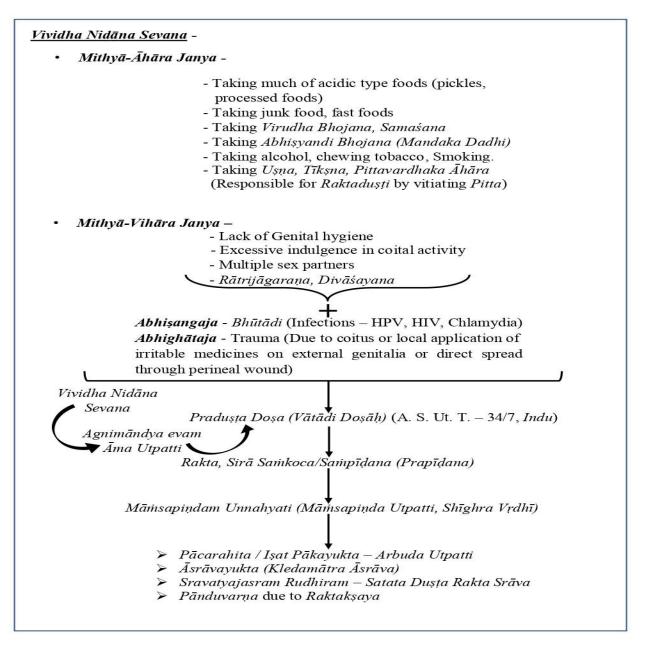


Chart No. 1. – Possible Pathogenesis based on different Nidānas