

## Cervical Cancer and its Various Emerging Impact

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### ABSTRACT

Cervical cancer, malignant neoplasm, appears in tissues of the cervix, a likely preventable disease that originates as the second most widespread malignancy in women. In spite of being considered as a treatable disease, 95% preventive and conditions that can be easily examined through Pap smear. This disease accounts for a miserable condition, probable 24 percent of India's cancer cases among women and in addition to that 80,000 Indian women die annually from the disease, which results from the unusual growth of cells in the cervix. No proper vaccination program from Indian government and miserable earning can be said responsible for this condition. Though the disease is both preventable and curable but still mortality rate in India is aggravating subsequently.

**Keywords:** cervix, HPV, DNA, Pap test, risk factors, naïve researches

### INTRODUCTION

Cervical cancer is a disease in which cancer cells gathering in the tissues of a woman's cervix. Most frequent symptoms are exaggerated vaginal discharged, Pelvic painfulness, Disconcert during sex. In a research deliberate by Laura Ungar (a recognized medical writer), every assemblage in India, 120,000 women get cervical person and 80,000 die of it.

Cervical cancer occurs when defective cells on the cervix develop out of hold. Cervical cancers can frequently successfully treat when it's recovered earlier. It is usually saved at a really stage through a Pap essay. Most adults screw been infected with HPV at any time. An infection may cure on its own. But every so often it can make genital warts or direction to cervical cancer. That's so it is necessary for women to make regular Pap tests. A Pap test can identify naïve changes in cervical cancer. On cure these cell changes and prevent one from cervical cancer. Cure to cervical cancer may differ with the stages of the disease. For first invasive stages of cancer, surgery is the

handling of prime. For encourage foster cases, radioactivity therapy along with chemotherapy is the topical standard of management.<sup>[1,2]</sup>

#### **Anatomy and physiology of the cervix:**

The cervix is the constricted, lower part of a women's uterus (womb). The cervix relates the primary body of the uterus with the vagina.

The cervix is segment of the female reproductive system, lower third portion of the uterus that forms the neck of the uterus and opens into the vagina which is also called the endocervical canal. The female reproductive system includes the internal organs vagina, ovaries, uterus and fertilization tubes (Fallopian tubes).

#### **Structure:**

The cervix is usually about 2 cm (1 inch) stressed. The cervix is outlined by the epithelium that is made of a thin layer of cells. Epithelial cells can be either squamous or columnar. It is divided into 2 main parts-

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Endocervix- the innermost conception of the cervix lining provides leading to the uterus.

Ectocervix- the outer side and lower rounded, lip-like portion of the cervix protrudes in the vagina.

The path from the uterus to the vagina is titled the endocervical furnish. Cells that origins the endocervical canal are typical glandular cells that secretes mucus. The columnar cells adheres the squamous cells in vicinity of the cervix titled the squamo-columnar junction. This vicinity also

termed as the transformation zone as the stately columnar cells are persistently being altered in flat squamous cells. It is in this transformation zone that precancerous alteration takes place and most cervical cancers vantage. Cervical cancer initiates easy alongside that the majority of cancer are squamous cell carcinomas, apparent in the squamous epithelial cells that row the cervix. Subsequent most widespread type is adenocarcinoma, emerging from glandular epithelial cells.

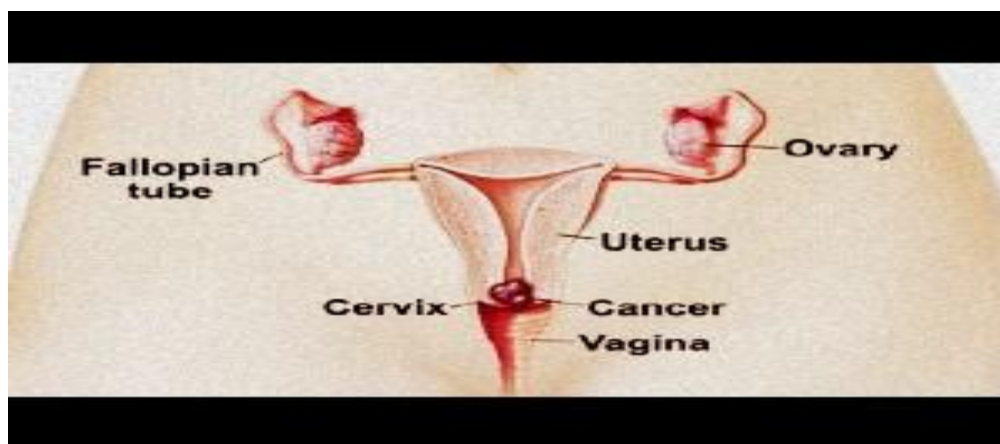


Fig. No. 1 Structure of women cervix<sup>[40]</sup>

#### Function:

The cervix attaches the body of the womb to the vagina. Each month – apart from during maternity or while a woman is in menopause – the inside layer of the uterus (endometrium) is lean-to through the cervix in the vagina, afterward out of the body. This development is called menstruation.

Splits of the liner of the cervix restrain mucus-secreting glands. Intended nearly all of the menstrual cycle, the mucus is bulky and does not permit sperm to penetrate. At ovulation, while a mature egg is freed from an ovary every month, the bulkiness of the mucus transforms and it conform the spermatozoa to pass through the cervix into the uterus. The cervix as well illustrates a significant role during

childbirth – it grants as a pathway connecting the uterus and the vagina.<sup>[3]</sup>

#### HPV

HPV is a grouping of diminutive DNA viruses that are frequently recovered in 70% – 80% of peoples earlier than they age 50. Fortunately nearly all of the cases do not result in cancer. Within the concerning 90% cases our body's immune system destroy HPV naturally in 1-2 years. Regrettably, sometime the virus endures in women for years. But in case HPV persist for 15-20 years, in that situation it converts normal cell to cancerous cell. Nearby 100+ types of HPV have been acknowledged. All these diverge minutely from one another in their genetic structure. 20-30 types grounds infection entirely to the lower genital tract.

In some recent researches it is found so, that the scientists discovered that whether decrement in HPV, dominance among 14–19 year-old girls may be because of direct immunity, they also discovered that vaccinated sexually active girls confirm a striking 88% diminish in occurrence of the relevant HPV strains, in comparison to the pre-vaccine era. However they additionally institute a 28% diminish in prevalence amid unvaccinated girls. The discovering was not statistically considerable, and was tricky to understand the differences in the detailed sexual behavior of the two groups — meant for illustration, the unvaccinated girls' tales fewer sexual partners. However, herd immunity is a probable explanation, and other studies have indicates that it is at play.

In the meantime, another study published "The Lancet" validates old findings that the jeopardy of cervical cancer is more in women who use the pill. That hazard fall back down to average levels within ten years after quitting the pill, they originate.<sup>[5]</sup>

As the artist Michael Douglas was truthful enough to concede in an interview, throat cancer that he was cured, for in 2010 is originate by HPV contracted via oral sex. (Douglas's representatives afterward unused to that he had deliberated the statement to refer to his hold particular case.)<sup>[2, 6]</sup>

### GENETIC SUSCEPTIBILITY

Cervical cancer is strongly related with transmission by oncogenic category of human papilloma virus (HPV). Although only a petite fraction of those infected produce cancer, indicating that remain factors lead to the advancement to cervical cancer. We have evaluated incidence of the disease in comparative of cases of cervical tumour as well as controls, and find a noteworthy familial gathering among biological, but not foster, relatives. We undergo no conflict in the assay to siblings whom mother or father are in common,

so the clustering would not be explained by steep transmission of HPV as of mother to child. These results present epidemiological evidence of a genetic inclination to cervical cancer.

Genetic susceptibility towards cervical cancer has been acknowledged via numerous studies on twins and first-degree relations, as considerable genome-wide linkage studies. Women with first degree biologic relative pursue two times additional risk of developing cervical cancer interrelated to women among no biologic first-degree individual with cervical cancer. Less to 1% cases of cervical cancer initiated inherited.

Relevantly, inheritance happens sporadically. In many studies it is initiated that cervical cancer can be approved as a division of a syndrome, Peutz-Jeghers syndrome symbolizes one such illustration. People suffering from this syndrome build up colored spots on skin, lips, and hands along with feet. These peoples moreover posses various being growth alongside their intestine, colon and stomach. The escalation may turn into cancerous with time.

The bumps can be easily observed in woman's cervix. In case these bumps turns cancerous, than it may be a type of inheritance of cervical cancer since it occur because of widen of her Peutz-Jeghers syndrome. Sign is evoked by transformation in the DNA of genome. If the change have taken place and oncogene form, then it may led to develop cancer and changes occurred by biological, chemical, nutritional or environmental aspects. Every so often our cells develops oncogene cell itself on misfortune. Same may happen in the meanwhile of replication or division. Auspiciously our cells gain ways to protect across DNA damage. In case, if unable to rehabilitate then apoptosis occurs and this helps cells to avoid from multiplying and probably leading to cancer.<sup>[2, 6, 7]</sup>

## **PATHOLOGY AND STAGING OF CERVICAL CANCER**

Pathology recommends the examination of tissue beneath a microscope in order to discover out in case it's cancerous or non-cancerous and the type of tumour it is. Diverged types of tumours can engage the cervix.

### **Benign tumours**

Benign tumours are non-cancerous cell expansion that limited to specified area and other parts of the body are not generally critical:

cervical polyp  
nabothian follicle  
uterine fibroid

### **Precancerous conditions**

Precancerous conditions pursue the potential to progress into cancer:

- cervical intraepithelial neoplasia
- squamous intra-epithelial lesion
- atypical glandular cells (AGC-neoplastic)

### **Malignant tumours**

Malignant tumours are cancerous development that has the prospective to metastasize (broaden to additional parts of the body):

- squamous cell carcinoma
- most widespread type (nearly 80–90% of cervical tumours)
- adenocarcinoma
- next most widespread type (nearly 10% of cervical tumours)

\* glassy cell carcinoma

- adenosquamous carcinoma
- malignant tumours
- lymphoma of the cervix
- adenoid basal epithelioma

\* melanoma of the cervix

\* carcinoid tumour

\* adenoid cystic carcinoma

\* small cell carcinoma

\* sarcoma of the cervix<sup>[3]</sup>

Subsequent to the type of tumour has been detected, the doctor will also reflect on:

- nonstandard the cancer cells appear and behave
- distant the cancer has developed
- extraordinary characteristics that may manipulate the course of the disease
- endurance statistics for the scrupulous type and stage of cancer

## **RESEARCH AND DEVELOPMENT IN CERVICAL CANCER**

Our awareness of cancer<sup>[3]</sup> is always intensifying. Surgeons and pathologist taking the advancement of enhanced research studies making our preventions, detect of cervical cancer and cure easy. In that situation we should be also be aware of naïve researches taking place and how we can make them beneficial to us to improve our quality of life. As we all know that our country is a major sufferer of cervical cancer curse.



Fig. No. 2 Awareness logo<sup>[40]</sup>

The following information's are collection of selective of researches showing blessing for cervical cancer.

### **RISK REDUCTION**

Initially, risk reduction is considered as it can be confirmed as foremost ground of cervical cancer. Following are strategies that help in reducing the probability of developing cervical cancer.

#### Remarkable research in risk reduction:

- Human papillomavirus (HPV) is the most widespread entity of cervical cancer. Particularly HPV-16 and HPV-18 are linked to most 70% of all cervical cancers.
- Gardasil is a vaccine that protects against most hazardous type of HPV: HPV-16, HPV-18, HPV-11 and HPV-6. Gardasil used to avoid precancerous transforms of the cervix origin by HPV-16, HPV-18 and comparable viruses in the alike family. Gardasil also avoids genital warts originated by HPV-6 and HPV-11.
- Cervarix is a vaccine that guard against HPV-16 and HPV-18.
- The producers of both vaccines counsel that the injections be specified 3 times over 6-month duration. Researchers are seeking to find out if smaller number doses of the vaccines can be procure to get the similar level of protection.<sup>[8]</sup>
- Researchers are also processing vaccines to impact HPV infections. These vaccines movement an insusceptible activity against the HPV-infected cells and may undo cervical cells with precancerous changes.<sup>[9]</sup>
- Cervical intraepithelial neoplasia (CIN) II and III are premalignant conditions of the cervix that develop in cervical cancer if left untreated. Women suffering with CIN II and III are frequently treated with surgery; nevertheless researchers are working on other non-surgical treatment alternatives. Imiquimod (Aldara, Zyclara) is a category of biological therapy in the strain of a topical ointment.
- Researchers are studying imiquimod as a possible treatment for CIN II and III (ASCO\*\*, Abstract 5041).

#### SCREENING

Researchers are working to improve screening techniques for precancerous conditions of the cervix and cervical cancer so that they can be found early and treated.

#### Remarkable research includes:

- The human papillomavirus (HPV) essay can conclude if a woman has assured high-risk category of HPV that can result to cervical cancer if left uncured. Numerous screening trials have revealed that HPV testing is more susceptible than cytology (Pap test) in perceiving a precancerous circumstance of the cervix known as cervical intraepithelial neoplasia.
- The United States American Cancer Society, for Colposcopy and Cervical Pathology affirm that there is adequate evidence to convey that women 30-65 years older, who asking to lengthen the screening duration from 3 to 5 years can do so with a amalgamation of screening with HPV as well as Pap testing.<sup>[10]</sup>
- A study in Canada shows that the HPV test could be superior to the Pap test the same as the primary screening tool of cervical cancer. This study is termed the HPV FOCAL study. Researchers also trust to come across out if the HPV test may consent to women to be screened less often. The study is currently ongoing in British Columbia for further study.<sup>[10]</sup>
- An enlarged randomized study in the Netherlands evaluated screening among both the HPV test and Pap test opposed to the only Pap test in women 29-56 years older. The study establish that screening with mutually the HPV and Pap tests led to prior detection of CIN II contrast to cytology. The study conducted in 2 rounds of testing, 5 years separately. Women who were originated to comprise CIN II or inferior in the first round were indulged. Researchers initiate that the group that suffer both HPV and Pap testing indicate a lower risk of enclose CIN III or cervical cancer within the

second round of testing match up to those who had Pap testing only.<sup>[11]</sup>

- American Cancer Society affirm that there is enough indication to confirm that women 30-65 years of age who craving to lengthen the screening interval from 3 to 5 years may do so with a combination of screening with HPV and Pap testing.<sup>[12]</sup>

- The ARTISTIC examination in the United Kingdom is attempting to discover out if it is riskless to hindrance cervical cancer screening in women having a negative HPV test. The experiment results advice that women having a negative HPV test may require 3 rounds of testing prior to it is safe to establish that cervical cancer screening may be expanded to 3 years in spite of being done more frequently. The ARTISTIC trial also according those long screening intervals may still be safe if the HPV test substitute the Pap test as of the primary screening test.<sup>[13]</sup>

- A spacious study in China opened that the HPV test can be utilized as a steadfast screening test for women in manifold age groups, embracing those younger to 35 years of age. Further research is needed to uncover that which age groups would achieve the majority benefit from this try.<sup>[14]</sup>

· Liquid-based Pap tests vary from predictable Pap tests in that assembles cervical cells are settled in a container of liquid, generally ethanol, instead of state smeared on a glass microscope slide. Some studies have publicized that liquid-based Pap tests are same sensitive in finding abnormal cells like as conventional Pap tests. Nevertheless, liquid-based Pap tests gain the benefit of being able to test for definite types of HPV with the same sample of cells.<sup>[10]</sup>

· International researchers seem at the prospect of women using home kits to assemble themselves their cervical cell samples for HPV testing. With having an optimism that this will

hearten more women to contribute in cervical cancer screening.<sup>[15]</sup>

· A processed Pap test uses a computer to inspect a cell sample and scratch areas of abnormal cells. The pathologist then captures a close look at the areas recognized by the computer. Many researches are requisite to find if computerized Pap tests will be an effective tool for cervical cancer screening.<sup>[16]</sup>

#### **DIAGNOSIS**

A key area of research activity involves developing better ways to diagnose and stage cervical cancer.

#### **Remarkable research includes:**

The Senital lymph nodes are the primary lymph node that a cancer cell goes through as cells spreads via the lymphatic system to complete body. Various studies are undergoing on sentinel lymph node biopsy (SLNB) for testing whereas this technique is truthful in determining or not cervical cancer distribute to the lymphatic nodes devoid of removing every lymph nodes. It might be utilized as a substitute to pelvic lymphadenectomy to bind the extent of surgery in women with premature stage of cervical cancer. Either radioisotope dye, blue dye otherwise both are injected before the surgery started. With the surgery begin, the surgeon recognize the sentinel lymph nodes and take out them. This procedure can also be utilized during laparoscopic surgery.<sup>[17]</sup>

#### **PROGNOSTIC FACTORS**

Prognostic factors that might assist to evaluate the outcome of the disease are undergoing study in cervical cancer. The Factors can be employed to forecast the chances of revitalization or of cancer approaching back. Doctors may perhaps also exercise prognostic factors to facilitate them make treatment suggestions.

#### **Remarkable research includes:**

· Sentinel lymph node biopsy can help doctors envisage prognosis in women by means of cervical cancer. Researchers have details that women suffering from cervical cancer that has extended to the sentinel lymph nodes possess a less favorable prognosis.<sup>[18]</sup>

· Clusterin is a protein related with programmed cell death. In a study establish that the existence of clusterin may be supportive in influential overall survival in women suffering with cervical cancer.<sup>[19]</sup>

· A study originate that a soaring level of vascular endothelial growth factor (VEGF) and receptor (VEGFR) along with a short level of the tissue inhibitor metalloproteinases 2 be linked with a low favorable results in women in the midst of cervical cancer. VEGFR is the receptor that binds to VEGF, a protein that encourage new blood vessels to figure. TIMP2 is thought to help prevent the spread of cancer.<sup>[20]</sup>

### TREATMENT

Researchers are superficial for new means to advance the treatment of cervical cancer. Enhancements in cancer management and new ways to manage the side effects related to treatment have improved the outlook and eminence of life for several people with cancer.

### Remarkable research includes:

· Laparoscopic radical hysterectomy is processes in which a slender, supple light tube and preoperative instruments are inserted through a little cut in the abdomen (laparoscopy) to take out the womb, cervix and surrounding lymph nodes. Studies demonstrate that laparoscopic radical hysterectomy may be a substitute to standard radical hysterectomy for treating emergent stage cervical cancer. There is informing that laparoscopic basal hysterectomy is related with inferior post-operative complications and a shorter retrieval than abdominal unit hysterectomy. Longer-term

follow-up is desirable to determine the safety and effectualness of the laparoscopic model.<sup>[21]</sup>

· Robotic radical hysterectomy is a type of laparoscopic radical hysterectomy. The surgeon sits close to the operating table and operates robotic arms to action the operation throughout several undersized cuts in the woman's abdomen. This technique (RRH) is being used to cure the women in the midst of cervical cancer.<sup>[22]</sup>

- Present practice has been effectively executed in women with phase IA1–IIA cervical cancer. Nearby, were slightest obstacle and the women were liberated from the hospital on the same date of their surgery. Studies have establish that robotic hysterectomy had a short operative time comparison to laparoscopy and was related with appreciably less blood loss and lesser complications than the typical approach, which is completed through a cut in the abdomen.<sup>[23]</sup>

- A study appears at survival pursuing robot-assisted surgery for untimely stage cervical cancer. The results illustrate lesser rates of reappearance and no distinction in overall survival when evaluated to open radical hysterectomy.<sup>[24]</sup>

- A study in Norway originate that robotic hysterectomy was association with a higher rate of recurrence evaluate to laparoscopic else abdominal hysterectomy.<sup>[25]</sup>

· Researchers are learning laparoscopic pelvic lymphadenectomy as a substitute to open pelvic lymphadenectomy, that exercise a larger incision. Mutually approaches are applied in women with premature stage cervical cancer to eliminate lymph nodes within the pelvis to observe if they restrain cancer. A study illustrates that laparoscopic pelvic lymphadenectomy be an effectual way to ensure for cancer inside the pelvic lymph nodes.<sup>[26]</sup> Further research is desired to establish how robotic surgical techniques may

contribute a role in care for women with cervical cancer into the future.

- A modified radical hysterectomy is a sort of surgery that eliminates lesser tissues and organs comparing to standard radical hysterectomy. The modified radical hysterectomy method consists of removable of the uterus, cervix, upper portion of the vagina and ligaments and tissues those compact envelop these organs. Lymph nodes are as well distant. Italian researchers establish that women who treated with modified radical hysterectomy in early stage cervical cancer confirm better sexual function following the surgery than women treated with a standard radical hysterectomy.<sup>[27]</sup>

- Doctors are working on a novel technique of hysterectomy termed as total mesometrial resection (TMMR) in women suffering with stage IB–IIB cervical cancer. TMMR eliminates the uterus together with portion of the neighboring tissue where cancer is aggravated likely to extend. In another study it is found that TMMR only (lacking adjuvant radiation therapy) can advance survival rates in women who generally would be cured with radical hysterectomy.<sup>[28]</sup>

- Radical trachelectomy is an option to radical hysterectomy intended for women of child-bearing age suffering with early stage cervical cancer those would prefer to preserve their fertility. With radical trachelectomy only the cervix is removed, the neighboring supporting ligaments along with the upper portion of the vagina. The remnants of the uterus and also the ovaries are remaining untouched. Surgeons are moreover treating with laparoscopic radical trachelectomy with high-quality results. Untimely studies have revealed that it is a secure and successful substitute to radical hysterectomy in women amid early stage cervical cancer.<sup>[29]</sup>

- Researchers are too working on robotic techniques for radical trachelectomy. According to a study women treated with robotic radical trachelectomy divulge lesser blood loss and a short hospital accommodation compared to women treated with an open radical trachelectomy.<sup>[30]</sup>

- Drugs entitled angiogenesis inhibitors blocker the creation of new blood vessels that a tumour requires to grow and stretch. Mainly cervical cancer cells formulate a protein known as vascular endothelial growth factor (VEGF). VEGF encourage the development of new blood vessels. Angiogenesis inhibitors like as bevacizumab and pazopanib, to treat cervical cancers are being study by researcher that express VEGF.<sup>[31]</sup>

- A stage III trial of the Gynecologic Oncology Group originate that women with repeated, metastatic IVA cervical cancer survive longer after bevacizumab was supplemented to chemotherapy with any cisplatin (Platinol AQ), paclitaxel (Taxol), paclitaxel moreover topotecan (Hycamtin) (ASCO, Abstract 03).

- A stage III clinical trial originate that generous gemcitabine (Gemzar) and cisplatin chemoradiation therapy followed by adjuvant gemcitabine and cisplatin enhanced survival in women in stage IIB–IVA cervical cancer contrast to typical cure of carboplatin (Paraplatin) or radiation therapy. Nevertheless, there were superfluous toxic side effects through the gemcitabine and cisplatin chemoradiation therapy regimen (Journal of Clinical Oncology, PMID 21444871).

- A stage II trial establish that pemetrexed (Alimta) along with cisplatin is favorable in curing advanced, determined or frequent carcinoma of the cervix. Present is good motive for supplementary study of this regimen within a phase III trial.<sup>[32]</sup>

- In learning establishes that neoadjuvant chemotherapy along with irinotecan



(Camptosar) and cisplatin prior to surgery is a successful treatment for women among locally advanced cervical cancer (cancer that has spread to restricted area). With neoadjuvant chemotherapy lesser cancer spread to the stroma is found. Nearby, also an inferior possibility of cancer at the surgical margin contrast to surgery only. Women those reported well to neoadjuvant therapy as well had minor rates of cancer extend to the pelvic lymph nodes comparison to women who did not reported well to the treatment.<sup>[33]</sup>

- Researchers are going through intensity-modulated radiation therapy (IMRT) to cure cervical cancer. IMRT avail computer technology to provide radiation from a series of diminutive beams of various strengths. In this approach, IMRT make the most of the radiation delivered to tumour cells whereas minimizes harm to normal adjacent tissues. Since less normal tissue obtain radiation with IMRT, women lean to have fewer side effects. Studies are as well looking at merge IMRT with chemotherapy or brachytherapy, that uses implants to convey radiation directly into or close to a tumour.<sup>[34]</sup>

- A study appears at treating women by early stage, intermediate-risk till high-risk cervical cancer. It establishes that healing with radical hysterectomy, chemotherapy along with cisplatin and IMRT is of advantage.<sup>[35]</sup>

- Researchers are making new approaches for merging external beam radiation therapy along with the platinum drug amalgamation, non-platinum drugs and also targeted drugs to heal cervical cancer.<sup>[36]</sup>

### Supportive care

Alive with cancer ought to be challenging in various ways. Compassionate care can help people cope suffering from cancer, its cure and inevitable side effects.

### Remarkable research includes:

- An examination sensing at toxicity, prognosticative factors and endurance in women who acknowledged concurrent chemoradiation for close by locally sophisticated cervical cancer. The outcome showed an excellent largely survival rate by a lesser rate of acute and also chronic side effects, demonstrating a good quality of life.<sup>[37]</sup>

- A level of lifespan quality of life study establish that, however women were pleased with their choice to have pelvic exenteration to cure a persistent gynecologic cancer, it was related with depression, deterioration physical and sexual performance and meager body image. Researchers are increasing interventions to progress quality of life in this assemblage of women.<sup>[38]</sup>

- Radiation therapy meant for cervical cancer may cause agonizing inflammation of the rectum and bladder. Various studies are being undergoing to learn hyperbaric oxygen therapy as an approach to supervise these curse effects in women suffering with gynecological cancers, along with cervical cancer. Hyperbaric oxygen therapy is specified with a special pressure chamber. In this method, a woman sits in the chamber, furthermore the pressure within is increased beyond the normal pressure of the atmosphere. On higher pressure, high levels of oxygen insert into a person's blood. And these high levels of oxygen helps to heal the damaged and infected tissues.<sup>[39]</sup>

### CONCLUSION

In this research paper I have given all my best efforts to make it easy and include most preferable researches. That can help one to beat cervical cancer and live an elite quality of life. Well, it is good says that "Prevention Is Better Than Cure", so we should follow this and go for Pap Smear test available in certain

hospitals. But in case if you find yourself as a sufferer, then better to take cure as soon as possible. Try to vaccinate your daughters or

sisters, to make their future more safe and secure.

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