

## Susceptibility to Cervical Cancer: An Overview

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### ABSTRACT:

**Background:** Cervical cancer imposes a huge global burden. The risk factors for cervical cancer have been the subject of numerous studies to date. The purpose of this study was to look into the global incidence, mortality, regional distribution, and risk factors for cervical cancer.

**Method:** To look for research published between 2000 and 2017, a literature search was carried out using PubMed, Web of Sciences, Scopus, and Google Scholar. Cervical cancer, cervix uteri cancer, risk factor, incidence, mortality, and combinations of these terms were among the keywords used.

**Result:** According to the study's findings, industrialized and developing nations have very different rates of cervical cancer incidence. The findings of this study demonstrated that a variety of factors, including sexually transmitted diseases, reproductive factors, hormonal influences, genetics, and host factors, contribute to the development of cervical cancer.

**Conclusion:** The results of this review study showed that a number of biological, economic, and health factors had an impact on the incidence of cervical cancer. Prevention programmes, a healthy lifestyle, giving up smoking, and timely and effective treatment of pre-cancerous lesions can prevent a considerable portion of cervical cancer.

**Keywords:** Cervical, Cancer, Risk, Findings, Infections, Health, Factors, Incidence.

### INTRODUCTION:

Cancer is today the second greatest cause of death worldwide, trailing only heart disease, and

this places a significant burden on societies Cancer and Organization, 2016<sup>1</sup>. Among the most prevalent cancers in women are gynecological cancers. The most prevalent type of gynecological cancer is cervical cancer. Indeed, it is a significant global public health issue and one of the leading contributors to disability-adjusted life years. However, one of the most

treatable cancers is cervical cancer. It is a common cause of death for women, especially in less developed countries. But thanks to recent information, the viral aetiology of cervical cancer has been well understood. This condition is one of the most avoidable cancers due to its slow growth, the presence of cytological evident lesions, and the development of effective treatments 2012 saw 528,000 new cases and 266,000 fatal cases of cervical cancer. Young adults are the age group with the highest prevalence of cervical cancer. Cervical cancer incidence and mortality rates have steadily declined worldwide. The death rate from cervical cancer in wealthy countries has dramatically declined as more cases are rapidly recognized. Numerous studies have shown that socioeconomic position significantly affects the prevalence, mortality, and survival rates of cervical cancer<sup>2</sup>. This has a number of implications, including screening access restrictions. Ineffective and insufficient treatment, the absence of prevention initiatives, and unhygienic settings.

Several epidemiological studies have demonstrated how several genetic factors influence the risk of acquiring cervical cancer. One of these is an HPV (human papilloma virus) oncogene type infection in the patient, which is the primary etiological cause in the development of this malignancy<sup>3</sup>. The most widespread STD in the world, HPV is strongly associated with cervical cancer. HPV testing and vaccination have just been available for the prevention of cervical cancer. For the prevention of cervical cancer, the identification of pertinent risk factors remains essential. Numerous research has been conducted on the risk factors for cervical cancer to date. This study's goal was to examine the incidence, mortality, regional distribution, and risk factors on a global scale.

## METHODOLOGY:

A literature search was done using PubMed, Web of Sciences, Scopus, and Google Scholar to discover papers that were published between 2000 and 2017. Cervical cancer, cervix uteri cancer, risk factor, incidence, mortality, or a combination of these terms were among the keywords utilized. The studies that gave a detailed description of the incidence and mortality rates of cervical cancer as well as any related risk factors were included in the current paper review study<sup>4</sup>.

## RESULTS:

Death and incidence: Cervical cancer is the fourth most prevalent cancer in women and the seventh most common cancer overall. In 2012, there were 528,000 new cases of cervical cancer. The likelihood of developing cervical cancer varies greatly by place. These tumors are found in less developed regions in about 85% of cases. Central and Eastern Europe, Southeast Asia, Latin America, and sub-Saharan Africa were shown to have the greatest incidence and fatality rates for cervical cancer. In Zimbabwe, Malawi, and Uganda, the prevalence of cervical cancer is more than twice as high as it is elsewhere. The incidence is lowest in Western Asia. The five countries with the highest percentage increases in cervical cancer diagnoses in 2012 were the Russian Federation (18,503), Brazil (18,503), China (61,619),

Indonesia (20,928), and India (122,844 cases) (15,342). Incidence rates of cervical cancer, age-standardized, ranged from 8.5 to 25.7 per 100,000 individuals in countries with high- to low-human development indices in 2012. Cervical cancer incidence is declining in several European and South American countries, North America, Oceania, and numerous Asian countries (such as Japan, China and India). In reality, the drop in cervical cancer incidence varies by region<sup>5</sup>. Cervical cancer is the third most prevalent malignancy that claims lives in low- and middle-income countries. Despite being rare in high-income countries, cervical cancer nevertheless claimed more than 266,000 lives worldwide in 2012, accounting for 7.5% of all fatalities from cancer in women. It is estimated that less developed regions account for nine out of ten cervical cancer fatalities. The fatality rate can vary between distinct geographic places by up to 18 times, with fewer than 2 per 100,000 in Western Asia, Western Europe, and Australia/New Zealand, but more than 20 per 100,000 in Melanesia and Middle and Eastern Africa. India accounts for 25% of cervical cancer fatalities. In many of the high incidence regions, like Africa, where screening rates for the disease are lower, women are most at risk for developing invasive cervical cancer. The average age-standardized death rate for cervical uterine cancer in countries with a high-to-low human development index is 6.8 per 100,000 people (range: 2.7 per 100,000 to 16.6 per 100,000)<sup>6</sup>.

The frequency and death of cervical cancer vary significantly by region. Some of the reasons that account for reported geographic differences include access to screening programmes (which allow for early detection and rapid treatment of precancerous lesions), the prevalence of HPV, and effective prophylaxis (such as the HPV vaccine). In high-income nations that have adopted and implemented screening programmes over decades, the incidence of cancer has fallen by 4% yearly and by a total of 70%. The incidence of cervical cancer, however, is rising or even increases in countries with poor screening, no screening, or low screening coverage. The socioeconomic diversity of nations has a substantial impact on compliance with screening programmes. Programs for screening and health promotion must take into account issues like insufficient funding for programme implementation, incomplete information, limited access to healthcare (due to financial, physical, or social barriers), psychosocial stress, and limited funding for screening and health promotion. The incidence of cancer has decreased by 4% annually and by a total of 70% in high-income countries that have adopted and implemented screening programmes over decades. However, in nations with inadequate screening, no screening, or low screening coverage, the incidence of cervical cancer is rising or even increasing. The socioeconomic diversity of countries has a significant impact on how well screening programmes are followed. Issues like insufficient funding for programme implementation, incomplete data, limited access to healthcare (due to financial, physical, or social barriers), psychosocial stress, and a lack of funding for screening and health promotion must all be taken into account by programmes for screening and health promotion. The HPV vaccine has been readily available for many years to help prevent and reduce the incidence of cervical cancer. Nevertheless, there are a few drawbacks to using this effective tactic, with the expense of vaccination in developing countries being the biggest

one. Sex, reproductive, and screening program quality issues can all have an impact on geographic disparities (laboratory and follow-up). Additional factors that contribute to the high incidence of cervical cancer in developing countries include inadequate cytological lesion detection and a failure to follow up on poor cytology results.

## **RISK FACTORS:**

### **Sexually transmitted diseases (STIs):**

#### **- Human Papilloma Virus (HPV)**

Infection with high-risk or oncogenic HPV strains is predominantly responsible for the development of precancerous and malignant cervical lesions. HPV 16 and 18 infections are the main causes of cervical cancer. High-risk variants, particularly HPV 16, have been found to be widespread in human populations. Sexual contact is usually how the disease, which causes squamous intraepithelial lesions, is transferred. After 6 to 12 months, the majority of lesions vanish due to immunological action. Meanwhile, a small number of these lesions are still present and have the potential to become cancer<sup>7</sup>. The age at which HPV is most frequent is 25, which may be related to changes in sexual behavior, according to a meta-analysis. In a meta-analysis study, the bimodal distribution of cervical cancer in specific regions was examined. Following a sexual contact, an HPV outbreak may be observed in this distribution. After reaching adulthood, there is a plateau, and the second peak is once again seen after the age of 45. As a result of a persistent infection with a high-risk type of HPV, cervical intraepithelial neoplasia gradually develops (CIN). The two viral oncoproteins E6 and E7 are the principal methods by which HPV contributes to carcinogenesis by interfering with the important tumour suppressor genes P53 and retinoblastoma. Changes in viral and host DNA methylation are also linked to E6 and E7. Interactions of E6 and E7 with cellular proteins and changes in DNA methylation control genetic integrity, cell adhesion, immunological response, apoptosis, and cellular regulation.

#### **Chlamydia trachomatis**

When invasive squamous cell carcinomas contain *C. trachomatis* DNA, the risk of cervical squamous cell cancer is increased. Serum antibodies to *C. trachomatis* are associated with a 1.8-fold greater risk of developing squamous cell carcinoma, according to the results of a case-control study carried out in seven different countries. More vulnerable groups include women under 55 and those with higher antibody titers. The impact of HPV on the host or the host's susceptibility to *C. trachomatis* infection may increase the risk of squamous cell carcinoma. Inflammation caused by chronic *C. trachomatis* as a result. Chlamydia trachomatis Studies demonstrated that prior *C. trachomatis* infection increases the risk of cervical squamous cell cancer. In this study, 40% of invasive squamous cell carcinomas had *C. trachomatis* DNA present. According to the findings of a case-control study conducted in seven different nations, serum antibodies to *C. trachomatis* are linked to a 1.8-fold increased risk of

developing squamous cell carcinoma. Women under 55 years old and those with greater antibody titers are more at risk. Infection with *C. trachomatis* may raise the risk of squamous cell carcinoma through increasing the host's sensitivity to HPV or the effects of HPV on the host<sup>10</sup>. Human immunodeficiency virus-positive women are more likely to get high-risk HPV strains (HIV). Studies on the relationship between HIV and cervical cancer have found that those who have HIV are more likely to develop CIN, invasive cervix cancer, abnormal Pap test findings, and persistent HPV infections with a variety of oncogene viruses. Herpes simplex virus (HSV). Serum HSV-2 antibodies are linked to invasive cervical cancer (or squamous cell carcinoma, adenocarcinoma, or adeno-squamous cervical carcinoma). However, there is no proof of these conclusions. For instance, the findings of a nested case-control study indicate that HSV-2 does not contribute to the emergence of cervical cancer.

## REPRODUCTIVE AND SEXUAL FACTORS:

### - Sexual partners

Cervical cancer risk has been linked to having multiple sexual partners. Generally speaking, the increased risk of HPV infection is to blame. However, the risk of cancer persisted even after accounting for HPV infection. As a result, persons who engage in several sexual relationships may be more susceptible to cancer for unrelated reasons. An earlier diagnosis may be related to older sexual experience, according to a theory. Young age at first sexual interaction is another risk factor for cervical cancer. Numerous studies have shown that full-term pregnancies increase the risk of invasive cervical cancer. High parity also increases a woman's risk of developing cancer. The risk of the disease and parity, but not the mother's age at her first pregnancy, were found to directly correspond in a collaborative international epidemiological study on cervical cancer. The risk of cervical cancer significantly increases with the number of deliveries. A cohort study with a follow-up of more than 13 years found that delivery was a predictor of CIN 3. This review study also found that delivery increased the risk of developing cervical cancer, particularly in women with high-risk HPV infections<sup>9</sup>. The recent and continued use of combination oral contraceptive (OC) methods increases the risk of cervical cancer. In a global collaborative epidemiological study of cervical cancer, longer OC use was linked to a higher relative risk for current users. Using the OC approach for five years or more, according to some reports, will increase your risk of getting cancer by double. However, among people who used just injectable progesterone for 5 years or longer, there is a small increase in the prevalence of invasive cervical cancer. Women who tested positive for HPV DNA had a threefold increased risk of getting cervical cancer if they used OCP for five years or more, according to a multi-center case control study. The results of this study showed that the initial use of OC medicines has no effect on the likelihood of developing cancer.



## BEHAVIORAL FACTORS:

### - Smoking

Numerous studies have shown that smoking is presently one of the leading risk factors for CIN 3 and invasive cervical cancer. There is a link between smoking in the past or present and cervical cancer. Those who stopped smoking for 10 years had a 50% lower risk of acquiring cancer than those who didn't, according to a significant cohort study. This study found no evidence that passive smoking increases the risk of cervical cancer. Instead, the age of the smoker is connected to the prevalence of cervical cancer. The results of a re-analysis of 23 epidemiological studies show that smoking cigarettes lowers the average age at which people start smoking and raises the risk of getting squamous cell carcinoma of the cervix. Smoking can increase the risk of cervical neoplasia in a variety of ways. One of the causes is the local activation of immune suppression by cigarette metabolites. Additionally, nicotine and its metabolites, which are tobacco-related chemicals, can damage the DNA of squamous cells. Smoking can affect the cervix's epithelium's epigenetic composition, which can promote the growth of neoplasia in that region of the body as well as many others.

## NUTRITIONAL AND DIETARY FACTORS:

Cervical cancer development is influenced by HPV infection, HPV persistence, HPV-related lesions, and cervical cancer progression. In recent years, there has been a lot of attention paid to the connection between dietary factors and the onset of cervical cancer. This problem has been examined in a number of research, however the findings are conflicting. In one study, higher intakes of green vegetables or dark green and yellow fruits as well as higher levels of - and -tocopherol were connected to a 50% decrease in CIN 3. Thus, eating a healthy, balanced diet leads to higher antioxidant levels and may therefore be associated to cervical neoplasia. Cervical cancer was found to substantially correlate with higher intakes of vitamin C, folate, vitamin E, beta-carotene, vitamin A, and lycopene, as well as vegetarian meals. The prevention of cervical cancer protection provided by dietary factors may be underpinned by molecular mechanisms. Two of the roles of vitamins C and E include increased mucosal response to infection and protection against free radicals and oxidants. Vitamins C and E help stop DNA adduct formation brought on by smoking. In addition to preventing viral multiplication and gene expression, antioxidants also regulate immune responses. Vitamins B12, folate, riboflavin, and thiamine may provide protection against precancerous lesions of the cervix. Consuming fruits strong in antioxidants on a daily basis lowers the risk of developing squamous intraepithelial lesions and lowers the incidence of cervical cancer, according to a nested case-control study. Beta-carotene, lycopene, zeaxanthin, retinol, and tocopherol blood levels were considerably lower in CIN and cervical cancer patients in a case-control study.

## INFLAMMATORY DISEASE:

Numerous studies have examined the potential link between inflammatory disorders and cervical cancer. According to the results of a population-based cohort study, women with rheumatoid arthritis and systemic lupus erythematosus are 1.5 times more likely to develop cervical cancer and cervical dysplasia. According to the results of a meta-analysis, people with systemic lupus erythematosus have a higher incidence of cervix neoplasia and a higher risk of developing cervical cancer. For example, lupus patients had a higher rate of abnormal Pap smears<sup>11</sup>It has been demonstrated that using immunosuppressive medications such as azathioprine and cyclophosphamide may make cervical cancer more common in these people. Contrarily, those with lupus have a decreased rate of cervical cancer screening.

## HOST FACTORS:

The role played by host genetic sensitivity in the genesis of cervical cancer has been the subject of numerous studies. In a case-control study, some genetic abnormalities in the host were connected to an increased risk of cervical cancer. Some polymorphisms have been connected to cellular immune responses or the processing of antigenic material. Two crucial stages in the cervical cancer pathogenesis—HPV persistence and disease development—could be impacted by host genetic differences.

### Prevention and vaccination

Our expanding knowledge of how HPV infection causes cervical cancer has led to the development of immunogenic, safe, and effective prophylactic vaccines. An HPV vaccination has been accessible since 2006. These immunizations are available in numerous nations across the world, despite the fact that vaccine coverage differs greatly between various regions. Sociocultural, health, and political difficulties are the major barriers to the use of this immunization in low-income and less developed countries. Currently, three different vaccinations are available on the market<sup>12</sup>.

#### - Quadrivalent vaccine(Gardasil)

This vaccine, which guards against HPV types 6, 11, 16, and 18, is composed of L1 recombinant protein particles that resemble viral particles (major capsid protein).

#### - Bivalent vaccine(Cervarix)

This vaccine defends against HPV types 16 and 18 by dispersing recombinant L1 capsid proteins in the form of viral-like particles.

#### - Nonavalent vaccine

This immunization was approved by the European Medicines Agency in June 2015 and the US Food and Drug Administration (FDA) in December 2014, respectively. This type of



vaccine, which protects against HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58, functions similarly to the bivalent and quadrivalent vaccines for a variety of targets. This specific vaccine provides close to 90% protection against cervical cancer and nearly 90% protection against genital warts. The patient is substantially protected against the HPV types that are included in the vaccines by these three vaccination types, which provide only sporadic protection against extra HPV types. Two doses of these vaccines are recommended for both sexes starting at age nine. For those above the age of 15, the vaccine is normally administered three times<sup>13</sup>.

## CONCLUSION:

This study set out to understand how various risk factors affected both the incidence and burden of cervical cancer. The study's findings show that cervical cancer incidence rates in industrialized and underdeveloped countries are considerably different from one another. Following the invention of the Pap smear test and the adoption of preventive vaccines, cervical cancer incidence rates considerably reduced in wealthier countries, but they kept rising in less developed countries. The considerable differences in cervical cancer incidence across different countries are mostly due to the existence, duration, and efficacy of screening programmes as well as changes in cervical cancer risk factors, notably those related to sexual activities. Cervical cancer is influenced by a variety of biological, socioeconomic, and health factors, according to the findings of several studies. The development of vaccinations as a means of reducing the disease's occurrence has been inspired by numerous research that have concentrated on the causal role of HPV in the development of cervical cancer. In addition to a variety of HPV oncogenes, there are other risk factors that can influence the occurrence of cervical cancer. Cervical cancer is more prevalent than other malignancies for a variety of reasons, including STIs, reproductive problems, hormonal problems, genetics, and host-related problems.

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