

Risk Factors for Cervical Cancer: An Epidemiological Review

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Abstract

Background: Cervical cancer is one of the most common female genital cancers. It accounts for about half of the one million new cases and one-quarter of all cancer deaths in women. The present study was designed to comprehensively identify the risk factors of cervical cancer using the results of similar studies.

Methods: The present study was an epidemiological review study. Searches related to the epidemiology and risk factors of cervical cancer between April 2020 and May 2020 were conducted by two researchers at four Latin scientific databases (Google Scholar, PubMed / Medline, Scopus, ISI Web of Science). The two researchers examined the extracted articles and included articles that referred to the epidemiology and risk factors of cervical cancer.

Results: The most important risk factors for cervical cancer included human papillomavirus, viral, fungal and bacterial infections, sexual behavior, smoking, pregnancy and childbirth, and other factors (family history and menopause earlier than 45 years).

Conclusion: It is recommended that health issues should be considered, especially during sexual intercourse, HPV screening in women, as well as periodic examinations for women.

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Introduction

Today, cancers are one of the major health problems in the world.¹ It is estimated that in 2018, there were about 9 million deaths from cancer.² Cervical cancer is the third most common cancer in women worldwide.³ Today, more than 85% of deaths related to cervical cancer occur in low-income and middle-income countries,⁴ and rarely occurs before age 20.⁴

Cervical cancer is one of the most common female genital cancers.¹ According to a 2012 GLOBOCAN report, the age-standardized rate of cervical cancer was estimated to be 14.0 per 100,000 population.⁵ It accounts for about half of the one million new cases and one-quarter of all cancer deaths in women. This cancer is developing in the world and is mainly seen in middle-aged women. In most European and North American countries, the incidence of cervical cancer deaths has dropped significantly over the past 40

years. This reduction is due to a combination of factors including improving genital hygiene and increase in condom use, improvements in treatment methods, and the beneficial effects of organized population-based cervical screening programs for early detection or diagnosis and introduction of HPV vaccines.⁶

Cervical cancer factors include co-infection with HIV, co-infection with chlamydia achromatic, reproductive factors, sexual behavior, obesity, diet, multi-parity and prolonged use of hormonal contraception. These cofactors have completely weak risks compared to oncogenic HPV persistence.⁶ Other factors that can play a role in cervical cancer are low economic status, lack of population awareness, and lack of screening and vaccination programs.⁸ Since so far, few studies have been conducted to identify the risk factors for cervical cancer, the present study was designed to identify the risk factors for cervical cancer.

Methods

The present study was an epidemiological review study. Searches related to the epidemiology and risk factors of cervical cancer between April 2020 and May 2020 were conducted by two researchers at four Latin scientific databases (Google Scholar, PubMed / Medline, Scopus, ISI Web of Science). Selected keywords for the search included “cancer”, “neoplasm”, “tumor”, “cervical”, “cervix”, “risk factor” and “epidemiology”. The articles were retrieved using advanced search and using AND and OR operators. The two researchers examined the extracted articles and included Persian and Latin articles on the epidemiology and risk factors of cervical cancer. Summaries of articles published in congresses and conferences were excluded from the study. Also, articles that did not have a full text were excluded. Initially, about 92 articles were obtained, and after applying the exclusion criteria and reporting the results, 41 articles were finally evaluated.

Results

Human Papillomavirus (HPV)

HPV infection is the most common and major risk factor for cervical cancer.⁹ This virus is known to be the most common sexually transmitted infection in the world.¹⁰ Before the virus was identified as the leading cause of cervical cancer, it was known to cause a variety of skin warts on different parts of the body.¹¹ HPV is a group of DNA-infected viruses that has more than 150 subtypes, and 12 types of viruses have been found for cervical cancer. Cervical cancer occurs in most patients as the result of infection with HPV16 and HPV18, with high-risk HPV16 being more common in populations. The virus can be transmitted quickly and easily, even through skin-to-skin contact and mucous membranes, from a carrier to a healthy person, with nearly 300 million people worldwide carrying the virus.¹²⁻¹⁵ HPV is associated with a variety of clinical conditions, ranging from harmless to advanced cancers. However, most HPV infections are benign.¹¹

Sexual intercourse usually transmits HPV, and infection with the virus causes lesions in the squamous cells. Most of these lesions last 6 to 12 months and are destroyed by the body's immune system, but few of these lesions remain and can lead to cancer.¹⁶ Women with HPV have the highest risk of developing cervical cancer.¹⁷ According to a study by Munoz et al., the DNA of this virus was found in 100% of patients with cervical cancer.¹⁸ However, this rate varied between 90 and 100 percent in other studies.¹⁹ In general, DNA of HPV is found in almost all patients with cervical cancer. However, the types of HPVs in these people were different.^{20, 21} Cervical cancer is specific to women, but because HPV is the

leading cause of the disease, both men and women are involved in the spread, epidemiological chain, and transmission. Also, although HPV is the leading cause of cervical cancer, it alone is not a sufficient factor and other factors are involved. Evidence of human papillomavirus has been found in almost all patients with cervical cancer and given the high similarity between the risk factors for HPV and cervical cancer, the risk factors for the virus and subsequent cervical cancer can be considered the same.^{22, 23}

Sexual Behaviors

Many epidemiological studies have shown that sexual behavior and sexual partners are the most important risk factors for the spread of HPV.²⁴ People's sexual behaviors (both male and female) can have a significant effect on increasing HPV and cervical cancer. A study in East Asia found that sexual activity and behavior were the most important risk factors for HPV outbreaks in areas where HPV prevalence was high. Also, women who had multiple sexual partners were at higher risk for HPV infection.²⁵ Another study from several Southeast Asian countries found that sexual behavior could increase the risk of cervical cancer. The study also found that the age of first sexual intercourse and having multiple sexual partners could be a factor in increasing the risk of cervical cancer. Regarding the age of first intercourse, it has been said that having the first sexual intercourse at the age of over 20 reduces the risk of cervical cancer.²⁶ A study by Suzanne et al. in Oceania and Australia found that younger sex and more sexual partners could have important and effective effects on the HPV virus.²⁷

One study looked at the risk factors for HPV, including young age at the onset of the first sexual intercourse, the number of sexual partners during life, and sexual contact with at-risk individuals. Also, due to the involvement of men in the spread of the virus and ultimately the indirect effect on cervical cancer, factors such as circumcision and proper use of condoms can reduce the risk of HPV infection.^{22, 28}

In a study by Xavier Bosch et al., the main risk factors for sexual behavior were cervical cancer prevalence, high number of sexual partners, young age at onset of sexual intercourse, and partner living with HPV. In addition, male sexual behaviors were determinants of the spread of this cancer.²⁴ In general, among sexual behaviors, young age when experiencing the first sexual intercourse, large number of sexual partners in women and incorrect sexual habits of men such as unprotected sex can have a great impact on the human papillomavirus infection, and, indirectly, it increases the risk of cervical cancer.²⁹⁻³¹

Smoking

Various studies have shown that smoking is one of the most important risk factors for cervical cancer.³² In

addition, smoking can be a risk factor for the persistence of HPV infection and the progression of the infection to cancer.²⁷ Smoking through various mechanisms can increase the risk of cervical neoplasia; one of these mechanisms is the local induction of immune system suppression by tobacco metabolites. In addition, the chemicals in cigarettes, such as nicotine and its metabolites, can cause DNA damage in the squamous cells and make them more vulnerable.³³ The study by Sugawara et al. found that the risk of cervical cancer was significantly higher in smokers. Although the average probability was reported in several studies, in general, a positive association between smoking and cervical cancer was confirmed.³⁴ One study found that women who smoked could increase their risk of cervical cancer twice as much as non-smokers and this increased risk increased with the intensity and duration of smoking.³⁵ Another study found that nicotine and tobacco smoke derivatives were found in the cervical mucus.³⁶ In general, many studies have shown that smoking, especially cigarette smoking, is a major risk factor for cervical cancer. The observation of the composition and derivatives of these substances in the cervical mucosa is evidence of this.^{37, 38}

Pregnancy and Childbirth

Other risk factors that can increase the risk of cervical cancer include multiple pregnancies, multiple births, and birth control pills. Taking oral contraceptives for 5 years or more, giving birth to 5 or more children, and having multiple, long-term pregnancies can increase the risk of cervical cancer. In another study, the birth of six or more children was considered a risk factor.³⁹ Also, according to a study of multiple and long-term pregnancies, overuse of birth control pills can play a role in the progression of HPV to cervical cancer.¹⁸ A study by Karimi Zarchi in Iran found that in 89% of people with cervical cancer, the first pregnancy occurred under the age of 20, and 86% of patients had more than five deliveries.⁴⁰

Other Infectious Agents

One study found that HPV was more common in women with a history of vaginal trichomoniasis, urinary tract infections (UTIs) and tuberculosis (TB).²⁵ A study also found that genital infections with chlamydia trachomatis, Herpes simplex virus, and genital warts could increase the risk of cervical cancer. Some of these infectious agents must be taken very seriously, so that the infection with chlamydia trachomatis has more than doubled since 2000-2006.^{24, 27, 41} A study by Koskela et al. showed that a history of chlamydia trachomatis infection helps to increase the risk of cervical cancer so that Chlamydia DNA was found in 40% of malignant invasive cells in uterine squamous tissue.⁴² Several studies have looked at the effects of HIV on cervical cancer, with HIV-positive

women having a higher risk of developing cervical cancer than HIV-negative women.⁴³⁻⁴⁵

Other Factors

In addition to the above points, other factors can also play a role. A diet low in fruits and vegetables is more likely to be contagious, and eating healthy foods that contain antioxidants can reduce the risk of cervical cancer.^{22, 46} The socio-economic situation is also influential, so that in better economic areas, the global incidence rate has been lower, but there have been exceptions in the Middle East and North Africa that could be due to religious beliefs in sexual behavior.⁴⁷ Obesity can also increase the chances of developing cervical cancer.

In Lacey et al.'s study, obese women (with a body mass index greater than 30) and overweight women (with a body mass index greater than 25) were twice as likely to develop it compared to other women.⁴⁸ Other causes, such as menopause before age 45 and a history of having a first-degree relative with cervical cancer, can increase the risk of cervical cancer.^{44, 49}

One of the major limitations of this study was the inaccessibility of the full text of many articles.

Conclusion

Cervical cancer is one of the most common cancers in women and has a number of risk factors, including human papillomavirus, viral, fungal and bacterial infections, sexual behavior, smoking, pregnancy and childbirth, and other factors (family history and menopause earlier than 45 years); therefore, it is recommended that health issues should be considered, especially during sexual intercourse, HPV screening in women, as well as periodic examinations for women.

Conflict of Interest: None declared.

References

- 1 Mokhtari AM, Riahi S, Fathalipour M, Delam H, Hashemnejad M, Hassanipour S. The age-standardized rate of female genital cancers in Iran: a systematic review and meta-analysis. *Journal of hayat*. 2018;24(3):204-19.
- 2 Fouladseresht H, Ghorbani M, Hassanipour S, Delam H, Abdzadeh E, Mokhtari AM, Mohseni S, Riahi S, Mohammadian-Hafshejani A, Salehiniya H. The incidence of non-hodgkin lymphoma in iran: a systematic review and meta-analysis. *World Cancer Research Journal*. 2019;6:http-apps.
- 3 Arbyn M, Weiderpass E, Bruni L, de Sanjosé S, Saraiya M, Ferlay J, et al. Estimates of incidence and mortality of cervical cancer in 2018: a worldwide analysis. *The Lancet Global Health*. 2020;8(2):e191-e203.

- 4 Bedell SL, Goldstein LS, Goldstein AR, Goldstein AT. Cervical Cancer Screening: Past, Present, and Future. *Sexual Medicine Reviews*. 2020;8(1):28-37.
- 5 Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. *International journal of cancer*. 2015;136(5):E359-E86.
- 6 Memon A, Bannister P. *Epidemiology of cervical cancer. Uterine Cervical Cancer*: Springer; 2019. p. 1-16.
- 7 Moscicki A-B, Schiffman M, Burchell A, Albero G, Giuliano AR, Goodman MT, et al. Updating the natural history of human papillomavirus and anogenital cancers. *Vaccine*. 2012;30:F24-F33.
- 8 Chan CK, Aimagambetova G, Ukybassova T, Kongrtay K, Azizan A. Human Papillomavirus Infection and Cervical Cancer: Epidemiology, Screening, and Vaccination—Review of Current Perspectives. *Journal of oncology*. 2019;2019.
- 9 Kuiava VA, Chielle EO. Epidemiology of cervix cancer in Brazil (2005-2015): study of mortality and hospital intervention rates. *Archives in Biosciences & Health*. 2019;1(1):45-60.
- 10 Weaver BA. Epidemiology and natural history of genital human papillomavirus infection. *Journal of the American Osteopathic Association*. 2006;106(Supplement 1):S2.
- 11 Burd EM. Human papillomavirus and cervical cancer. *Clinical microbiology reviews*. 2003;16(1):1-17.
- 12 Alves C, Alves L, Lunet N. Epidemiology of cervical cancer. *Cancer*. 2007;55:32.
- 13 Marrazzo JM, Koutsky LA, Kiviat NB, Kuypers JM, Stine K. Papanicolaou test screening and prevalence of genital human papillomavirus among women who have sex with women. *American journal of public health*. 2001;91(6):947.
- 14 Bruni L, Diaz M, Castellsagué M, Ferrer E, Bosch FX, de Sanjosé S. Cervical human papillomavirus prevalence in 5 continents: meta-analysis of 1 million women with normal cytological findings. *Journal of Infectious Diseases*. 2010;202(12):1789-99.
- 15 Bouvard V, Baan R, Straif K, Grosse Y, Secretan B, El Ghissassi F, et al. A review of human carcinogens—Part B: biological agents. *The Lancet Oncology*. 2009;10(4):321.
- 16 Zur Hausen H. Papillomaviruses and cancer: from basic studies to clinical application. *Nature reviews cancer*. 2002;2(5):342-50.
- 17 Ondrusova M, Zubor P, Ondrus D. Time trends in cervical cancer epidemiology in the Slovak Republic: reflection on the non-implementation of screening with international comparisons. *Neoplasma*. 2012;59(2):121-8.
- 18 Munoz N, Castellsagué X, de González AB, Gissmann L. HPV in the etiology of human cancer. *Vaccine*. 2006;24:S1-S10.
- 19 Walboomers JM, Jacobs MV, Manos MM, Bosch FX, Kummer JA, Shah KV, et al. Human papillomavirus is a necessary cause of invasive cervical cancer worldwide. *The Journal of pathology*. 1999;189(1):12-9.
- 20 Paul SB, Tiwary BK, Choudhury AP. Studies on the Epidemiology of Cervical Cancer in Southern Assam. *Assam University Journal of Science and Technology*. 2011;7(1):36-42.
- 21 Smith JS, Lindsay L, Hoots B, Keys J, Franceschi S, Winer R, et al. Human papillomavirus type distribution in invasive cervical cancer and high-grade cervical lesions: a meta-analysis update. *International journal of cancer*. 2007;121(3):621-32.
- 22 Castellsagué X. Natural history and epidemiology of HPV infection and cervical cancer. *Gynecologic oncology*. 2008;110(3):S4-S7.
- 23 Castellsagué X, Bosch FX, Muñoz N. The male role in cervical cancer. *salud pública de méxico*. 2003;45:345-53.
- 24 Bosch FX, de Sanjosé S. The epidemiology of human papillomavirus infection and cervical cancer. *Disease markers*. 2007;23(4):213-27.
- 25 Shi JF, Qiao YL, Smith JS, Dondog B, Bao YP, Dai M, et al. Epidemiology and prevention of human papillomavirus and cervical cancer in China and Mongolia. *Vaccine*. 2008;26 Suppl 12:M53-9.
- 26 Domingo EJ, Noviani R, Noor MRM, Ngelangel CA, Limpaphayom KK, Van Thuan T, et al. Epidemiology and prevention of cervical cancer in Indonesia, Malaysia, the Philippines, Thailand and Vietnam. *Vaccine*. 2008;26:M71-M9.
- 27 Garland SM, Brotherton JM, Skinner SR, Pitts M, Saville M, Mola G, et al. Human papillomavirus and cervical cancer in Australasia and Oceania: risk-factors, epidemiology and prevention. *Vaccine*. 2008;26:M80-M8.
- 28 Bleeker MC, Hogewoning CJ, Voorhorst FJ, van den Brule AJ, Snijders PJ, Starink TM, et al. Condom use promotes regression of human papillomavirus-associated penile lesions in male sexual partners of women with cervical intraepithelial neoplasia. *International Journal of Cancer*. 2003;107(5):804-10.
- 29 Schiffman MH, Brinton LA. The epidemiology of cervical carcinogenesis. *Cancer*. 1995;76(S10):1888-901.
- 30 Franco EL, Duarte-Franco E, Ferenczy A. Cervical cancer: epidemiology, prevention and the role of human papillomavirus infection. *Cmaj*. 2001;164(7):1017-25.
- 31 Louie K, De Sanjose S, Diaz M, Castellsague X, Herrero R, Meijer C, et al. Early age at first sexual intercourse and early pregnancy are risk factors for cervical cancer in developing countries. *British journal of cancer*. 2009;100(7):1191-7.
- 32 Momenimovahed Z, Salehiniya H. Incidence, mortality and risk factors of cervical cancer in the world. *Biomedical Research and Therapy*. 2017;4(12):1795-811.
- 33 Roura E, Castellsagué X, Pawlita M, Travier N, Waterboer T, Margall N, et al. Smoking as a major

- risk factor for cervical cancer and pre-cancer: Results from the EPIC cohort. *International journal of cancer*. 2014;135(2):453-66.
- 34 Sugawara Y, Tsuji I, Mizoue T, Inoue M, Sawada N, Matsuo K, et al. Cigarette smoking and cervical cancer risk: An evaluation based on a systematic review and meta-analysis among Japanese women. *Japanese journal of clinical oncology*. 2019;49(1):77-86.
 - 35 Brinton LA, Schairer C, Haenszel W, Stolley P, Lehman HF, Levine R, et al. Cigarette smoking and invasive cervical cancer. *Jama*. 1986;255(23):3265-9.
 - 36 Schiffman MH, Haley NJ, Felton JS, Andrews A, Kaslow RA, Lancaster WD, et al. Biochemical epidemiology of cervical neoplasia: Measuring cigarette smoke constituents in the cervix. *Cancer Research*. 1987;47(14):3886-8.
 - 37 Kjellberg L, Hallmans G, Åhren A, Johansson R, Bergman F, Wadell G, et al. Smoking, diet, pregnancy and oral contraceptive use as risk factors for cervical intra-epithelial neoplasia in relation to human papillomavirus infection. *British journal of cancer*. 2000;82(7):1332-8.
 - 38 Melikian AA, Sun P, Prokopczyk B, El-Bayoumy K, Hoffmann D, Wang X, et al. Identification of benzo [a] pyrene metabolites in cervical mucus and DNA adducts in cervical tissues in humans by gas chromatography-mass spectrometry. *Cancer letters*. 1999;146(2):127-34.
 - 39 Domingo EJ, Echo D. Epidemiology, prevention and treatment of cervical cancer in the Philippines. *Journal of gynecologic oncology*. 2009;20(1):11-6.
 - 40 Zarchi MK, Akhavan A, Gholami H, Dehghani A, Naghshi M, Mohseni F. Evaluation of cervical cancer risk-factors in women referred to Yazd-Iran hospitals from 2002 to 2009. *Asian Pacific Journal of Cancer Prevention*. 2010;11:537-8.
 - 41 Brotherton JM. How much cervical cancer in Australia is vaccine preventable? A meta-analysis. *Vaccine*. 2008;26(2):250-6.
 - 42 Koskela P, Anttila T, Bjørge T, Brunsvig A, Dillner J, Hakama M, et al. Chlamydia trachomatis infection as a risk factor for invasive cervical cancer. *International journal of cancer*. 2000;85(1):35-9.
 - 43 Blaise NYH, Cedric TF. Descriptive epidemiology of uterine cervix cancer at the medical oncology unit of the Yaoundé general hospital-Cameroon. *GSC Biological and Pharmaceutical Sciences*. 2019;9(1):083-91.
 - 44 Hillemanns P, Soergel P, Hertel H, Jentschke M. Epidemiology and early detection of cervical cancer. *Oncology research and treatment*. 2016;39(9):501-6.
 - 45 Louie KS, De Sanjose S, Mayaud P. Epidemiology and prevention of human papillomavirus and cervical cancer in sub-Saharan Africa: a comprehensive review. *Tropical Medicine & International Health*. 2009;14(10):1287-302.
 - 46 Ghosh C, Baker JA, Moysich KB, Rivera R, Brasure JR, McCann SE. Dietary intakes of selected nutrients and food groups and risk of cervical cancer. *Nutrition and cancer*. 2008;60(3):331-41.
 - 47 Negrin LGC. Epidemiology of cervical cancer in Latin America. *ecancermedicalsecience*. 2015;9.
 - 48 Lacey Jr JV, Swanson CA, Brinton LA, Altekruse SF, Barnes WA, Gravitt PE, et al. Obesity as a potential risk factor for adenocarcinomas and squamous cell carcinomas of the uterine cervix. *Cancer: Interdisciplinary International Journal of the American Cancer Society*. 2003;98(4):814-21.
 - 49 Chatterjee S, Chattopadhyay A, Samanta L. HPV and cervical cancer epidemiology-current status of HPV vaccination in India. *Asian Pacific Journal of Cancer Prevention*. 2016;17(8):3663-73.