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The Etiology and Epidemiology Exploration of Cervical Cancer

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Abstract Cervical cancer is a common gynecological malignancy that predominantly affects young women, posing serious threats to women's health and lives. Studies in etiology and epidemiology have revealed the relationship between HPV infection and cervical cancer, marking a significant breakthrough in its prevention and treatment. HPV vaccines and screening technologies have been widely applied in clinical practice, substantially reducing the incidence and mortality rates of cervical cancer. Furthermore, research has identified associations between cervical cancer occurrence and development with factors such as smoking, high-fat diets, and vitamin deficiencies. To enhance the treatment effectiveness and prevention of cervical cancer, China needs to bolster fundamental research and clinical practice. In future studies, China should further explore other factors associated with cervical cancer and devise corresponding treatment and prevention strategies. Strengthening fundamental research and clinical practice to improve treatment effectiveness and prevention levels constitutes a crucial task for the present and future. The purpose of this review is to foster a better understanding of cervical cancer, its etiology, and contributing factors, contributing to cervical cancer treatment and prevention efforts while drawing greater attention to women's health.

Keywords Cervical cancer; HPV infection; Etiology; Epidemiology

Cervical cancer is one of the most common malignancies among women and a significant global women's health issue according to statistics from the International Agency for Research on Cancer, approximately 500 000 women worldwide die from cervical cancer each year. In developing countries, cervical cancer remains a leading cause of female mortality. Although the mortality rate from cervical cancer has significantly decreased in developed nations, there still exists a notable incidence and mortality rate. Hence, studying the etiology and epidemiology of cervical cancer holds crucial significance in devising better preventive and therapeutic strategies.

The occurrence of cervical cancer is associated with various factors, primarily the human papillomavirus (HPV) infection. Additionally, other elements such as genetic predisposition, long-term contraceptive use, early onset of sexual activity, multiple pregnancies, smoking, among others, can influence cervical cancer development. Therefore, exploring the etiology of cervical cancer can deepen our understanding of its pathogenesis, facilitating the search for new treatment and prevention approaches. Epidemiological studies of cervical cancer are equally vital. Disparities in cervical cancer incidence and mortality rates across different regions and populations are linked to socio-economic factors, educational levels, and healthcare services. Understanding the patterns of cervical cancer epidemiology can assist in formulating more targeted preventive and treatment strategies.

Research into cervical cancer holds significant importance concerning health issues, prevention and control, etiological investigations, early diagnosis, and treatment. Continual in-depth research enables better comprehension and management of this serious public health concern. By thoroughly investigating the etiology and epidemiology of cervical cancer, we can provide more accurate and effective strategies for prevention and control, ultimately reducing its incidence and mortality rates, and make contributions to women's health and social development. This review aims to explore the etiology and epidemiology of cervical cancer, providing readers with comprehensive insights to better understand its mechanisms and patterns. This understanding serves as a basis for scientifically informed preventive and treatment strategies.

1 Etiological Study of Cervical Cancer

1.1 Relationship between HPV virus and cervical cancer

The Human Papilloma virus (HPV) is a DNA virus transmitted through sexual contact, primarily responsible for the occurrence of cervical cancer. The extent and types of HPV infections lead to varying degrees of cervical lesions. Among them, high-risk HPV types (such as HPV16, 18) are the primary pathogens causing cervical cancer. The longer the duration of HPV infection, the higher the risk of cervical cancer development.

HPV is prevalent and infects a wide range of individuals. In sexually active women, the incidence of HPV infection can exceed 70%. Although most people will clear themselves after being infected with HPV, some people may develop cervical cancer after infection. Hence, HPV infection stands as a major factor contributing to the development of cervical cancer (Schiffman et al., 2007).

There are many mechanisms between HPV infection and cervical cancer, mainly including the following aspects: HPV virus infection can cause atypical proliferation of cervical epithelial cells, thereby forming cervical lesions. High-risk HPV types disrupt the gene expression in cervical cells, prompting cell proliferation and transformation, ultimately forming cancerous cells. HPV infection also inhibits the autophagy and apoptosis of cervical cells, thereby enhancing the survival and proliferation of cancer cells (Figure 1).
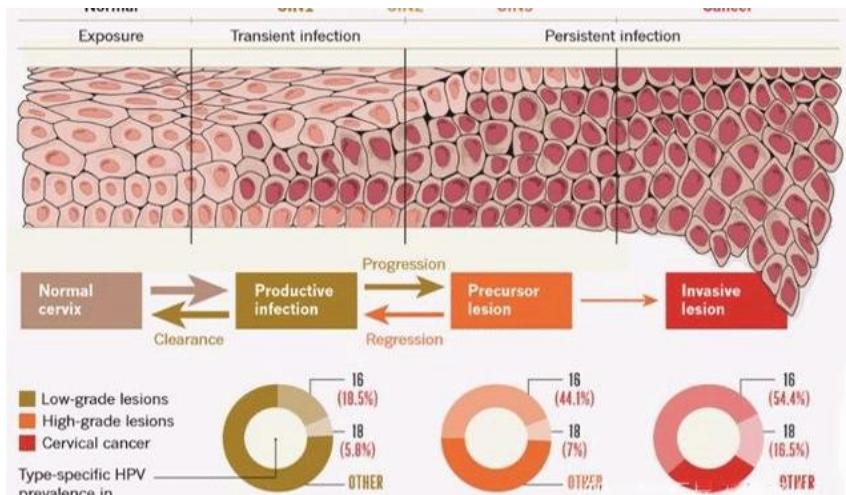

Figure 1 The development process of cervical cancer (Source: https://zhuanlan.zhihu.com/p/63054607)

At present, there are multiple HPV vaccines available in the market that effectively prevent HPV infection and the occurrence of cervical cancer. HPV vaccines can prevent infections caused by high-risk HPV types, thereby reducing the risk of cervical cancer. According to relevant research data, receiving the HPV vaccine can decrease the incidence of cervical cancer by over 70%. Additionally, screening and treating HPV infe ctions are crucial measures for preventing and treating cervical cancer. Currently, the World Health Organization recommends cervical cancer screening for women aged 20 to 65, which includes Pap smears and HPV testing. If cervical abnormalities or HPV infections are detected, timely treatment is necessary to prevent the progression of lesions into cervical cancer. HPV infection stands as one of the primary factors leading to cervical cancer. HPV vaccines, screening, and treatment are crucial means of preventing and treating cervical cancer, effectively reducing the risk of its occurrence (Zhou et al., 2023).

1.2 Genetic factors and cervical cancer incidence

Genetic factors also play a role in the occurrence of cervical cancer. Some studies suggest an increased risk of developing cervical cancer for individuals with a family history of the disease. Moreover, specific gene mutations are associated with cervical cancer. For instance, mutations in the *BRCA1* gene can elevate the risk of developing cervical cancer. *BRCA1* is a tumor suppressor gene that inhibits tumor formation by regulating pathways involved in DNA repair and cell apoptosis. Mutations in *BRCA1* may compromise its tumor-suppressing function, thereby

increasing the risk of cervical cancer. Research indicates that individuals with *BRCA1* gene mutations have 2-3 times higher risk of developing cervical cancer compared to the general population.

Furthermore, other gene mutations may also be linked to cervical cancer. For example, mutations in the *MLH1* gene could heighten the risk of cervical cancer, while the absence of the *GSTT1* gene might potentially reduce the risk. Future studies focusing on genetic aspects are necessary to explore the impact of gene mutations on cervical cancer occurrence, aiding in the development of more targeted preventive and therapeutic strategies. Currently, some genetic testing companies offer mutation tests targeting genes like *BRCA1*, enabling women to understand their risk of cervical cancer for more precise preventive and treatment measures.

Genetic factors are significant influencers in the development of cervical cancer. Mutations in genes like *BRCA1* can increase the risk of developing cervical cancer, and genetic testing can help women understand their susceptibility to cervical cancer for more precise preventive and therapeutic approaches. Apart from genetic factors, various other elements such as dietary habits, lifestyle, and environmental pollution may affect gene expression, indirectly impacting cervical cancer occurrence. Further research into these factors' impact on gene expression and function is crucial for better prevention and treatment of cervical cancer (Trimble et al., 2015).

1.3 Other related factors
1.3.1 Long-term use of oral contraceptives
There is a certain correlation between long-term use of oral contraceptives and the incidence of cervical cancer. Studies have found that the risk of developing cervical cancer increases in women who have used oral contraceptives for more than 5 years. The mechanism of oral contraceptives involves suppressing ovulation to prevent pregnancy. However, long-term usage might also affect the growth and differentiation of cervical epithelial cells, thereby increasing the risk of cervical cancer.

1.3.2 Early initiation of sexual activity
The early initiation of sexual activity is associated with the occurrence of cervical cancer. During adolescence, the cervix is not fully mature, making it less resistant to pathogens and more susceptible to infections. Additionally, early initiation of sexual activity might lead to dysplasia in cervical epithelial cells, further increasing the risk of cervical cancer. Multiple pregnancies are also linked to the incidence of cervical cancer. Research indicates that multiple pregnancies can elevate the risk of developing cervical cancer, possibly due to the damage and repair processes in cervical epithelial cells caused by multiple pregnancies, consequently increasing the risk of cervical cancer.

1.3.3 Smoking and other factors
Smoking is another significant factor contributing to cervical cancer. Studies suggest that smoking increases the risk of cervical cancer, possibly because carcinogens in tobacco can directly or indirectly affect the growth and differentiation of cervical epithelial cells. Besides the mentioned factors, various other elements such as immune function, nutritional status, among others, might influence cervical cancer occurrence.

Further research is needed to explore the impact of these factors on cervical cancer incidence to develop more precise preventive and treatment strategies. In summary, long-term use of oral contraceptives, early initiation of sexual activity, multiple pregnancies, smoking, and other factors could influence cervical cancer occurrence. Understanding these related factors can help women take effective preventive measures to reduce the risk of cervical cancer. Moreover, future research is crucial to delve deeper into the mechanisms behind cervical cancer occurrence to provide more accurate preventive and treatment measures.

2 Factors Influencing the Incidence and Mortality of Cervical Cancer
Cervical cancer is one of the important health issues for women worldwide. It is a malignant tumor that is related to multiple factors in its occurrence and development. Annually, over 500 000 women globally succumb to cervical cancer, with a majority occurring in low and middle-income countries. The global annual incidence of

cervical cancer is around 15 to 20 cases per 100 000 individuals, with a mortality rate of 8 to 10 cases per 100 000 individuals. In high-income countries, the incidence and mortality rates of cervical cancer are relatively lower. Disparities exist in these rates among different regions and demographics. Higher rates in low to middle-income countries correlate with factors like healthcare services, preventive measures, and screening access. Strengthening global awareness, promoting preventive measures like screenings and vaccinations among women, can effectively reduce cervical cancer incidence and mortality. Moreover, enhancing healthcare services and coverage on a global scale is essential to offer comprehensive and superior health services to women. Additionally, further research into cervical cancer's etiology and treatment methods is necessary to provide more effective means for prevention and treatment (Bosch et al., 2022).

Some studies indicate that socioeconomic factors significantly influence cervical cancer incidence and mortality. Incidence and mortality rates are higher in low and middle-income countries compared to high-income countries, possibly due to inadequate healthcare services, preventive measures, and screening in these countries. Additionally, educational attainment is linked to cervical cancer incidence and mortality. Research suggests that women with higher education levels have a lower risk of cervical cancer. This could be attributed to the higher likelihood of health education acceptance and screenings among educated women, aiding in the early detection and treatment of cervical cancer. Healthcare services are also among the significant factors impacting cervical cancer incidence and mortality. Studies suggest that improving the coverage and quality of screening and treatment effectively reduces cervical cancer incidence and mortality. Moreover, vaccination stands as an effective method for preventing cervical cancer, yet its accessibility remains lower in low and middle-income countries.

Although cervical cancer has high global incidence and mortality rates, advancements in medical technology and preventive measures are gradually improving this situation. For example, enhancements in screening and treatment technologies effectively prevent and treat cervical cancer, and vaccination remains an effective preventive measure. In addition, global promotion and popularization, raising women's health awareness, can also help reduce the incidence and mortality of cervical cancer. Variations in cervical cancer occurrence exist across regions and demographics, associated with factors like age, ethnicity, and reproductive history. Factors influencing cervical cancer incidence and mortality include socioeconomic status, education, and healthcare services. Future efforts should focus on global awareness campaigns, enhancing women's health consciousness, promoting preventive measures like screenings and vaccinations to reduce cervical cancer occurrence and mortality. Simultaneously, bolstering global healthcare services and coverage to provide comprehensive and superior health services to women is essential (Arbyn et al., 2020).

3 Future Research Directions

3.1 Strengthening fundamental research for innovative therapeutic and preventive strategies

Cervical cancer's prevention and treatment remain a global challenge. While China has acquired certain treatment and prevention strategies, substantial work lies ahead. Thus, intensifying fundamental research on cervical cancer etiology to explore novel treatment and prevention strategies becomes imperative.

In-depth exploration of the relationship between HPV infection and cervical cancer occurrence is crucial for China. This entails uncovering fresh treatment and prevention approaches. While HPV vaccines serve as a vital preventive measure, not all individuals can access them. Hence, China needs further research into HPV infection treatments, exploring novel vaccines and therapies. Additionally, elucidating the HPV virus's mechanisms of action, specifically its impact on cell proliferation and apoptosis, is necessary to identify new treatment and prevention strategies.

Augmenting research on other factors and their correlation with cervical cancer, such as lifestyle, environmental influences, and genetics, is pivotal. Studying the impact of these factors on cervical cancer will facilitate the exploration of relevant treatment and prevention strategies. For instance, research could examine the preventive role of dietary improvements and lifestyle changes in cervical cancer or delve into the impact of environmental pollution, enabling the formulation of appropriate prevention and treatment strategies.

Advancing studies in genetics, metabolism, and immunology is crucial to unearth new treatment and prevention strategies. Research into genetic variations and expressions concerning cervical cancer development could pave the way for targeted treatment strategies. Similarly, exploring the relationship between metabolites, immune factors, and cervical cancer could reveal potential treatment and prevention avenues. Strengthening fundamental research in cervical cancer etiology to explore new treatment and prevention strategies is critical for its prevention and control. Continuously exploring innovative treatment and prevention strategies can enhance the cure and survival rates of cervical cancer, offering patients more hope and possibilities (Gao and Zhang, 2023).

3.2 Enhancing screening and diagnostic techniques for prevention and treatment
Early screening and diagnosis play a vital role in preventing and treating cervical cancer, requiring continued improvement in techniques. While there have been significant advancements in cervical cancer screening and diagnostic technologies, numerous challenges persist, demanding further enhancement of their accuracy and reliability.

China needs to research more precise and effective HPV screening techniques to further improve the accuracy and reliability of HPV screening. At present, commonly used HPV screening techniques include liquid thin-layer cytology, HPV-DNA detection, and protein chips. These technologies have been widely applied in clinical practice, but there are still some problems, such as high false positive and false negative rates, complex operations, etc., which need to be improved in accuracy and reliability (Huh et al., 2015; Chuang et al., 2016).

Exploration of more sensitive and specific diagnostic techniques like liquid-based cytology, biomarkers, and imaging is vital to improve early diagnosis rates and treatment outcomes for cervical cancer. Although liquid-based cytology has seen significant accuracy improvements, issues persist, such as a high false-positive rate and diagnostic results influenced by collected cell quantity and quality. Hence, there's a need for further refinement. Biomarkers and imaging are essential research areas. Biomarkers, detecting specific proteins, genes, or metabolites, offer high specificity and sensitivity. Imaging technologies like magnetic resonance imaging and ultrasound can determine tumor location, size, morphology, and its relationship with surrounding tissues. While these technologies are extensively used clinically, further research and refinement are needed to enhance their accuracy and reliability. Furthermore, promoting and popularizing advanced treatment and surgical techniques like microwave therapy, laser treatment, and surgical excision are essential to improve treatment effectiveness and survival rates. These techniques are widely used clinically but require further research and improvement to enhance efficacy and safety (Cuzick et al., 2008; Pfaendler and Tewari, 2016).

Enhancing screening and diagnostic techniques for cervical cancer prevention and control is critical. Continuous exploration of new technologies and methods to improve their accuracy and reliability is necessary to provide better treatment and recovery for patients. Simultaneously, strengthening healthcare professionals' training and education to enhance their understanding and treatment levels for cervical cancer is essential to offer patients comprehensive and superior medical services (Table 1).

Table 1 Preventive screening in women of different age groups

Population (Age)	Recommended screening methods	Propose
<21	No screening	-
21~29	Cytology was screened individually every 3 years	-
30~65	None (Best), or cytology alone every 3 years (acceptable)	HPV screening alone is not recommended
>65	If the previous screening has sufficient negative results, there is no need to screen again	If the previous screening has sufficient negative results, there is no need to screen again
Female gender after the hysterectomy	No screening is required	For women with no cervix and no CIN 2, CIN 3, adenocarcinoma or cervical cancer
Women vaccinated with the HPV vaccine	Follow the screening strategy for the corresponding age	-

3.3 Strengthening social awareness and health education to enhance preventive measures

Boosting awareness and understanding of cervical cancer within the public sphere is crucial. It's necessary to enhance education on cervical cancer prevention, screening, and raise awareness among women regarding health preservation. Additionally, emphasizing information about cervical cancer treatments and rehabilitation is vital to help patients understand the disease better, thereby improving treatment outcomes and survival rates. Moreover, bolstering healthcare professionals' training and knowledge on cervical cancer will enable them to offer comprehensive and superior medical services to patients.

Cervical cancer prevention and treatment require a concerted effort from society as a whole. Future research directions and prospects need to address multiple facets. Strengthening fundamental research in cervical cancer etiology to explore new treatment and prevention strategies can offer more choices and possibilities for its prevention and control. Enhancing screening and diagnostic technologies for cervical cancer can improve accuracy and reliability, thereby providing better treatment and recovery for patients. Strengthening social awareness and health education to elevate people's health consciousness and preventive measures is a critical step for preventing and controlling cervical cancer, constituting a long-term task in its prevention and treatment. We believe that with efforts from across society, future advancements and achievements can contribute significantly to preventing and treating cervical cancer.

4 Summary and Outlook

Etiological and epidemiological studies have highlighted the close relationship between HPV (Human Papillomavirus) infection and the occurrence and development of cervical cancer. HPV infection stands as one of the primary causes of cervical cancer, especially high-risk HPV types like HPV16 and HPV18. Consequently, preventing HPV infection is among the essential measures to prevent cervical cancer. HPV vaccines, an effective method to prevent HPV infection, are already widely used clinically. Simultaneously, HPV screening serves as an important preventive measure, enabling the early detection and treatment of HPV infection and early cervical cancer lesions (Li et al., 2023).

Etiological and epidemiological research has revealed the relationship between cervical cancer and various other factors. Studies indicate a close association between factors such as smoking, high-fat diet, vitamin deficiency, long-term oral contraceptive use, low parity, and having multiple sexual partners with the occurrence and development of cervical cancer. Therefore, lifestyle improvements, reduced environmental pollution, and avoidance of genetic factors are also crucial measures for preventing cervical cancer. Through pathological and molecular biology studies of cervical cancer, a better understanding of the disease's mechanisms and molecular characteristics can lead to more precise and personalized treatment plans. Moreover, epidemiological research has highlighted differences in treatment response and prognosis among different populations, guiding the formulation of more scientific and rational treatment approaches. In the future, there is a need to further strengthen basic research and clinical practice to explore new treatment and prevention strategies, offering more hope and opportunities for preventing and treating cervical cancer. Enhancing both basic research and clinical practice is imperative to improve the efficacy of cervical cancer treatment and prevention (Wright et al., 2002; Li and Kong, 2023).

Basic research serves as the foundation for enhancing the treatment effectiveness and prevention levels of cervical cancer. It's crucial to delve further into the mechanisms of HPV infection, encompassing the virus's impact on host cells and the immune response of the host to viral infection. Simultaneously, exploring the relationship between other factors and the occurrence of cervical cancer is essential for formulating corresponding treatment and prevention strategies. Factors such as genetics, environment, and others play pivotal roles in influencing the occurrence and development of cervical cancer. Therefore, further research into these factors' correlation with cervical cancer is necessary to devise suitable treatment and prevention strategies. Public health education and awareness campaigns are integral in elevating cervical cancer prevention standards. It's essential to disseminate preventive knowledge about cervical cancer through various channels, including measures to prevent HPV infection, lifestyle adjustments, and the significance of regular check-ups, among others. Additionally, there's a

need to intensify screening and management for high-risk populations, promptly identifying and treating early-stage lesions to reduce the incidence and mortality rates of cervical cancer. Strengthening both basic research and clinical practices stands as a critical task in elevating the treatment effectiveness and prevention standards of cervical cancer, both in the present and the future. We need to constantly explore and innovate, work together, and make greater contributions to the treatment and prevention of cervical cancer.

Acknowledgments

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