REVIEW ARTICLE

Evidence from clinical studies on prevention and treatment of cervical cancer through nutrological management: a systematic review

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Abstract

Introduction: Cervical cancer is the second leading cause of death among women of childbearing age worldwide. In 2020, an incidence of 604,000 and 342,000 deaths were estimated. Possible primary preventive strategies include diet and dietary supplements. **Objective:** This was to conduct a systematic review to clarify the main scientific evidence from clinical studies on the prevention and treatment of cervical cancer through nutritional triggers and nutrology. **Methods:** The systematic review rules of the PRISMA Platform were followed. The search was conducted from February to May 2025 in the Scopus, PubMed, Science Direct, Scielo, and Google Scholar databases. The quality of the studies was based on the GRADE instrument and the risk of bias was analyzed according to the Cochrane instrument. **Results and Conclusion:** A total of 81 articles were found. A total of 20 articles were evaluated in full and 15 were included and developed in the present systematic review study. Considering the Cochrane tool for risk of bias, the overall assessment resulted in 31 studies with a high risk of bias and 24 studies that did not meet GRADE and AMSTAR-2. Most studies showed homogeneity in their results, with $X^2=89.8\%>50\%$. It was concluded that a diet rich in plant-based nutrients may be important in reducing the risk of cervical cancer. Adherence to the Mediterranean diet reduces the risk of cervical cancer by 60%. Changes in dietary habits may contribute to preventing the onset of cervical cancer by 30% to 40%. The consumption of sugary drinks is associated with type II endometrial cancer. The consumption of fruits and vegetables reduces the risk of cervical cancer. Vitamin D may exert beneficial actions in the early stages of cervical cancer, preventing its onset and progression. Lactobacillus strains isolated from human breast milk may be considered a topical drug with a potential therapeutic index due to their efficacy against cervical cancer cells.

Keywords: Cervical cancer. Nutrition. Diet. Prevention. Treatment.

Introduction

Cervical cancer is the second leading cause of death among women of childbearing age worldwide. In 2020, 604,000 and 342,000 deaths were estimated [1]. According to GLOBOCAN data for 2020, Latin America and the Caribbean ranked second in the world in incidence and mortality, with 59,439 new cases and 31,582 deaths [2]. It has been suggested that the incidence in these low- and middle-income countries may be due to several factors, including diet and lifestyle [3].

In this regard, several factors have been shown to influence the risk of persistent human papillomavirus (HPV) infection and tumor progression [4]. In this sense, cervical carcinoma is a major health problem worldwide, being the second most common cancer among women, ranking first in many developing countries. Several important epidemiological risk factors have been identified as contributing to the development of this condition. Of fundamental importance is HPV infection, which is the major risk factor [4].

There are evolving primary and secondary preventive strategies that may further reduce the burden

of cervical carcinoma. Potential primary preventive strategies include risk reduction, diet or dietary supplements, HPV vaccines, and other chemopreventive agents. Potential advances in secondary preventive strategies include new technologies for Pap smears, HPV typing screening, and other adjuvant screening procedures. The impact of these strategies will depend on the evidence to support their use, along with the characteristics of the population and environment in which they are used [4,5].

The natural history of cervical cancer suggests that prevention may be achieved by modifying the host immune system through a nutrient-mediated program. There is a preventive role for dietary intake in human papillomavirus (HPV)-induced cervical intraepithelial neoplasia (CIN). High fruit and vegetable intake appears to be protective against CIN. The findings also highlight the possibility of consuming high levels of specific nutrients, vitamins, and minerals and retaining sufficient levels of these elements in the body, especially those with high antioxidant and antiviral properties, to prevent the progression of transient and persistent HPV infections to high-grade CIN 2 and 3 [3-5].

Although it appears that the intake of specific nutrients, vitamins, and minerals may be beneficial in preventing CIN, there is a lack of evidence from controlled trials to confirm this. Healthcare professionals should focus on implementing a balanced diet prevention strategy at an early stage for cervical cancer prevention [5,6].

Given this, the present study performed a systematic review to clarify the main scientific evidence from clinical studies of cervical cancer prevention and treatment through nutritional triggers and nutrology.

Methods

Study Design

This study followed the international systematic review model, following the PRISMA (preferred reporting items for systematic reviews and meta-analysis) rules. Available at: http://www.prisma-statement.org/?AspxAutoDetectCookieSupport=1. Accessed on: 05/21/2025. The AMSTAR-2 (Assessing the methodological quality of systematic reviews) methodological quality standards were also followed. Available at: https://amstar.ca/. Accessed on: 05/21/2025.

Search Strategy and Search Sources

The literature search process was carried out from February to May 2025 and developed based on Scopus, Embase, PubMed, Science Direct, Scielo, and Google Scholar, covering scientific articles from various periods

to the present day. The following health science descriptors (DeCS/MeSH Terms) were used: "Cervical cancer. Nutrition. Diet. Prevention. Treatment", and the Boolean "and" between MeSH terms and "or" between historical findings were used.

Study Quality and Risk of Bias

Quality was classified as high, moderate, low, or very low regarding the risk of bias, clarity of comparisons, precision, and consistency of analyses. The most evident emphasis was on systematic review articles or meta-analyses of randomized clinical trials, followed by randomized clinical trials. Low quality of evidence was attributed to case reports, editorials, and brief communications, according to the GRADE instrument. The risk of bias was analyzed according to the Cochrane instrument by analyzing the Funnel Plot graph (Sample size versus Effect size), using Cohen's d test.

Results and Discussion
Summary of Findings

A total of 81 articles were found and submitted to eligibility analysis, with 15 final studies selected to compose the results of this systematic review. The studies listed were of medium to high quality (Figure 1), considering the level of scientific evidence of studies such as meta-analysis, consensus, randomized clinical, prospective, and observational. Biases did not compromise the scientific basis of the studies. According to the GRADE instrument, most studies presented homogeneity in their results, with $X^2=89.8\%>50\%$. Considering the Cochrane tool for risk of bias, the overall assessment resulted in 31 studies with a high risk of bias and 24 studies that did not meet GRADE and AMSTAR-2.

Figure 1. Selection of the articles.
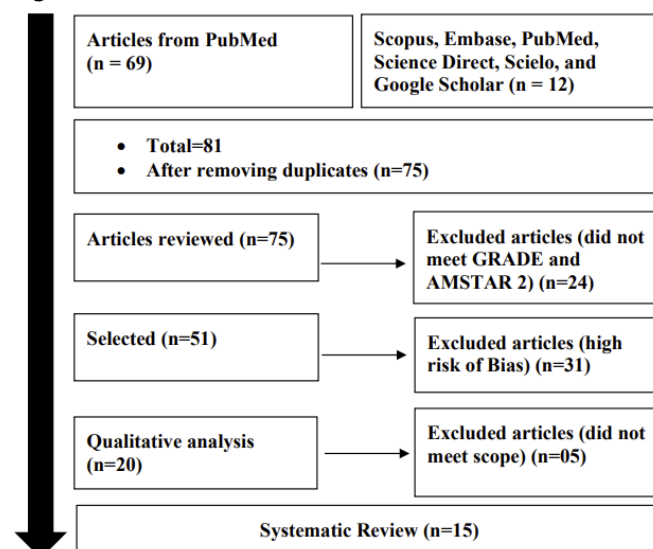
Source: Own authorship.

Figure 2 presents the results of the risk of bias of the studies using the Funnel Plot, showing the calculation of the Effect Size (Magnitude of the difference) using Cohen's Test (d). Precision (sample size) was determined indirectly by the inverse of the standard error (1/Standard Error). This graph had a symmetrical behavior, not suggesting a significant risk of bias, both among studies with small sample sizes (lower precision) that are shown at the bottom of the graph and in studies with large sample sizes that are shown at the top.

Figure 2. The symmetrical funnel plot suggests no risk of bias among the studies with small sample sizes that are shown at the bottom of the graph. Studies with high confidence and high recommendation are shown above the graph (n=15 studies).
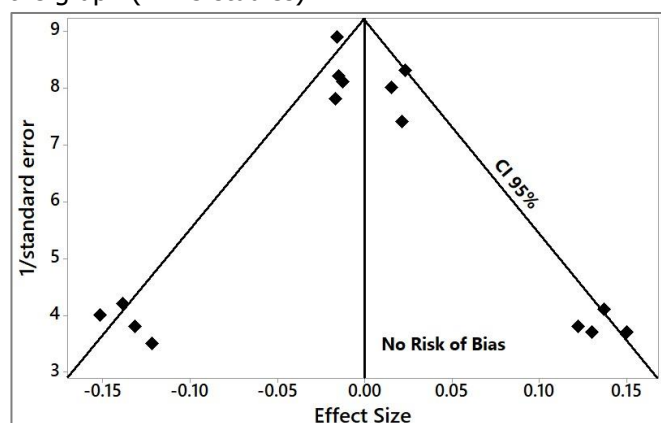
Source: Own authorship.

Clinical Results

The incidence rate of cervical cancer (cervical cancer) has been increasing worldwide, especially in countries with a high Human Development Index (HDI) [7]. This rate is influenced by aging, population growth, and changes in cancer risk factors, some of which are related to socioeconomic development [8]. Regarding dietary patterns, a study established that adherence to the Mediterranean diet reduces the risk of cervical cancer by 60% while following a Western diet represents a risk factor for its onset [9]. It is estimated that changes in dietary habits can contribute to preventing the onset of cervical cancer by 30% to 40% [10].

A diet high in sugar generally leads to weight gain and metabolic parameters associated with obesity, insulin resistance, steroid hormone bioactivity, oxidative stress, inflammation, and the development and progression of cancer [11]. According to Inoue-Choi et al. [12], the consumption of sugar-sweetened beverages is associated with type II endometrial cancer. Thus, the incidence of cervical cancer in this region may be associated with the consumption of sugary drinks.

The authors Najafi et al. [13] showed that a high intake of fruits and vegetables can reduce the risk of cervical cancer. Furthermore, the risk of cervical cancer was lower in patients with high scores on the healthy diet pattern, while Hajiesmaeil et al. [14] found that patients with cervical cancer had lower intake of fruits and vegetables. Furthermore, Hwang et al. [15] found that consumption of fruits and vegetables reduces the risk of cervical cancer (OR = 2.84, 95% CI 1.26 to 6.42, p = 0.06 for vegetables; OR = 2.93, 95% CI 1.25 to 6.87, p = 0.01 for fruits). All this is possible due to the antioxidants that fruits and vegetables contain, such as vitamin C and a- and b-carotene, which limit the damage caused by free radicals [16].

Furthermore, vitamin D, together with its active metabolite calcitriol and its metabolic and signaling system known as the vitamin D endocrine system, has been widely recognized as an essential regulator of calcium homeostasis, in addition to non-calcemic antitumor effects in a variety of human cancers, including cervical cancer. Several studies have found an inverse relationship between the incidence of cervical neoplasia and vitamin D levels. Although an optimal vitamin D status helps in the prevention and regression of lowgrade squamous intraepithelial lesions of the cervix, it appears that vitamin D alone or in combination with chemotherapeutic agents has little efficacy once advanced cervical cancer is established. These observations suggest that an optimal vitamin D status may exert beneficial actions in the early stages of cervical cancer, preventing its onset and progression [17].

In addition, a cross-sectional clinical study developed by the authors Kim et al. (2021) [18] investigated the correlation of coffee consumption and physical exercise with cancer. Participants ≥40 years old in the Korean Genome and Epidemiology Study 2004–2016 were included (n = 162,220). Histories of gastric cancer, liver cancer, colon cancer, breast cancer, cervical cancer, lung cancer, thyroid cancer, prostate cancer, and bladder cancer were analyzed according to coffee consumption groups using logistic regression models. The odds among individuals in the group who consumed more than 60 cups of coffee/month were lower for gastric cancer (adjusted odds ratio (aOR) = 0.80 (95% confidence intervals = 0.65– 0.98)), liver cancer (0.32 (0.18–0.58)), colon cancer (0.53 (0.39–0.72)), breast cancer (0.56 (0.45–0.70)), and thyroid cancer (0.71 (0.59–0.85)) than for individuals in the no-coffee group. Physical exercise of ≥150 min/week was correlated with increased odds of gastric cancer (1.18 (1.03-1.36)), colon cancer (1.52 (1.26-1.83)), breast cancer (1.53 (1.35-1.74)), thyroid cancer (1.42 (1.27-1.59)), and prostate cancer (1.61 (1.13-2.28))

compared with no exercise. Coffee consumption was associated with a reduced risk of gastric cancer, liver cancer, colon cancer, breast cancer, and thyroid cancer in the adult population. Physical exercise was positively correlated with gastric cancer, colon cancer, breast cancer, thyroid cancer, and prostate cancer.

Nutrient deficiencies have also been repeatedly associated with cervical human papillomavirus (HPV) persistence, cervical neoplasia, and cervical cancer in case-control studies. A prospective observational cohort study examined the relationship between overall diet quality and dietary components with spontaneous resolution of cervical HPV over 1 year. Women with low-grade cervical cytology and/or a positive HPV test completed a 24-hour dietary recall, from which the Healthy Eating Index (HEI)-2010, an overall diet quality score, and food category scores were calculated. Participants were treated clinically according to national treatment guidelines. Those whose subsequent tests demonstrated normalization of cytology and/or HPV testing (HPV resolution) were compared with those whose abnormalities persisted or progressed (HPV nonresolution). A total of 26 women were included in the HPV resolution group and 38 in the nonresolution group. They were observed for a median of 428 and 412 days, respectively (p = 0.09). There was no difference in overall diet quality between groups. Intake of total and whole fruits, and seafood/vegetable protein were associated with HPV resolution in a logistic regression model (all p < 0.05) [19].

Authors analyzed the relationships between intake of selected dietary nutrients, food groups, and cervical cancer risk in a hospital-based case-control study including 239 cases diagnosed with squamous cell carcinoma of the cervix and 979 hospital patients with non-neoplastic diagnoses who completed a self-administered questionnaire. Significant risk reductions of approximately 40-60% were observed for women in the highest tertiles vs. lower dietary fiber (OR=0.59, 95% CI=0.37-0.94), vitamin C (OR=0.52, 95% CI=0.33-0.80), vitamin E (OR=0.44, 95% CI=0.27-0.72), vitamin A (OR=0.47, 95% CI=0.30-0.73), alpha-carotene (OR=0.41, 95% CI=0.27-0.63), beta-carotene (OR=0.44, 95% CI=0.29-0.68), lutein (OR=0.51, 95% CI=0.33-0.79), folate (OR=0.55, 95% CI=0.53-0.79). CI=0.34–0.88) and total fruit and vegetable intake (OR=0.52, 95% CI=0.34–0.77) [20].

Finally, lactic acid bacteria have been categorized as probiotics and play a crucial role in human health by stimulating nutrient supply, shaping the immune system, and preventing colonization of pathogenic microbes. A study analyzed the mechanisms of action of the probiotic strains *Lactobacillus casei* SR1, *Lactobacillus casei* SR2, and *Lactobacillus paracasei* SR4

isolated from human breast milk. The bioactivity of the cell-free culture supernatant (CFCS) secreted by these strains on the cervical cancer cell line (HeLa) was also evaluated using cytotoxicity assay and apoptosis analysis. The results demonstrated that these newly isolated Lactobacillus strains from human milk exhibited remarkable probiotic characteristics, such as excellent antibiotic susceptibility, excellent antioxidant activity, and promising resistance to low pH and high concentrations of bile salts. The results of the conducted bioactivity assays verified that CFCSs had acceptable anticancer effects on cervical cancer cells (HeLa) by upregulating the expression of the apoptotic genes BAX, BAD, caspase3, caspase8, and caspase9 and downregulating the expression of the BCl-2 gene [21].

Conclusion

It was concluded that a diet rich in plant-based nutrients may be important in reducing the risk of cervical cancer. Adherence to the Mediterranean diet reduces the risk of cervical cancer by 60%. Changes in dietary habits may contribute to preventing the onset of cervical cancer by 30% to 40%. Consumption of sugary drinks is associated with type II endometrial cancer. Fruit and vegetable consumption reduces the risk of cervical cancer. Vitamin D may exert beneficial actions in the early stages of cervical cancer, preventing its onset and progression. Lactobacillus strains isolated from human breast milk may be considered as a topical drug with a potential therapeutic index due to their efficacy against cervical cancer cells.

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No additional data are available.

Conflict of Interest

The authors declare no conflict of interest.

Similarity Check

It was applied by Ithenticate®.

Application of Artificial Intelligence (AI)

Not applicable.

Peer Review Process

It was performed.

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