



# Association of Breast Cancer with Human Papilloma Virus Infection: A Systematic Review

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## ABSTRACT

**Introduction:** Breast cancer (BC) is the most common tumor among women throughout the world in both developed and developing countries. In 2024, an estimated 310,720 women and 2,800 men will be diagnosed with invasive BC. This condition accounts for 12.5% of all new annual cancer cases worldwide, making it the most common cancer in the world. Viruses are considered an interesting but controversial etiological risk factor for BC, which can precipitate tumorigenesis via synergy with other environmental factors. There is evidence that viral DNA from viruses such as human papillomavirus (HPV) can be found in BC samples, as well as in healthy tissue samples. As there is conflicting evidence regarding the relationship between BC and HPV, in this review article, we focused on the association of BC with HPV Infection.

**Search Strategy:** Based on PRISMA guidelines, we performed a comprehensive search of pertinent databases, including PubMed, Scopus, Google Scholar, and Web of Science, with the keyword “HPV”, “Human Papillomavirus Virus”, “Human Papillomaviruses”, “Breast Cancer”, “Breast Neoplasm”, and “Breast Tumor” from 2008 to 2022. There was no language restriction, and studies investigating the presence of HPV DNA or proteins in BC tissues or blood samples were considered except for book chapters, conference abstracts, theses, press articles, narratives, and systematic reviews. According to the inclusion and exclusion criteria, 24 case-control studies were initially identified.

**Results:** 24 records, 15 from PubMed and 9 from Google Scholar, Scopus, and Web of Science, were collected. Different methods were used to detect HPV across studies. PCR for DNA detection and immunohistochemistry for protein expression analysis were the most frequent methods employed. Among the studies, 14 reported a positive association between HPV infection and BC, while 10 found no significant correlation. The prevalence of HPV in BC ranged from 0 % to 86.2%, which HPV-16 and HPV-18 were the main cause. However, some studies confirmed the presence of low-risk types of HPV, such as HPV-6 and HPV-11, in BC samples.

**Conclusion and Discussion:** Our findings reveal the positive role of HPVs in BC. Since some other studies do not find any evidence of this relationship, the difference in study design, sample size, and geographical locations may be the reason for varying results. Future studies with larger sample sizes and standardized diagnostic methods are needed to clarify the precise role of HPV in BC. If the role of HPV in BC is determined, HPV vaccines could be used for BC prevention and immunotherapy.

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