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REVIEWS

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Association of endometriosis with human papillomavirus (HPV) infection: a systematic review

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A – Study Design, **B** – Data Collection, **C** – Statistical Analysis, **D** – Data Interpretation, **E** – Manuscript Preparation, **F** – Literature Search, **G** – Funds Collection

Summary Endometriosis is defined as the presence of endometrial tissue outside of the uterine cavity. It is a chronic disease affecting approximately 10% of women. In addition to producing a vast array of symptoms, including chronic pelvic pain and dysmenorrhea, the condition significantly impacts quality of life. Over the past century, several theories have attempted to explain the pathogenesis of this complex disease. Recent studies have investigated the potential role of human papillomavirus (HPV) infection in the development of endometriotic lesions. The objective of this review was to conduct a search of online databases (Embase, Medline and PubMed) for available literature from June 2013 to June 2023 concerning the association between HPV and endometriosis. After screening 110 articles, 23 studies met the eligibility criteria, and 8 were included in the systematic review. Out of the 8 reviewed papers, 3 described a statistically significant correlation between HPV infection and endometriosis. 3 others only demonstrated a higher incidence of HPV infection in patients with confirmed endometriosis. A difference in the dominant type of HPV serotype among patients diagnosed with endometriosis was also observed. Given these results, it is difficult to propose a viral origin of the disease. Further research is necessary to determine the role of HPV infection in the development of endometriosis.
Key words: endometriosis; papillomavirus infections, viral sexually transmitted diseases.

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Background

Endometriosis is a chronic inflammatory disease that affects 5–10% of women of reproductive age worldwide [1]. It is a debilitating condition characterised by symptoms such as chronic pelvic pain, dysmenorrhea, dyspareunia, dysuria and infertility [2]. Traditionally, endometriosis has been defined as the surgical detection of endometriotic tissue outside of the uterine cavity [3]. However, there has been a recent shift towards a more patient-focused definition that considers its complex, chronic and systemic nature. This updated understanding takes into account the involvement of various tissues, as well as the cellular and molecular origins of the disease [4].

Endometriosis not only has significant physical effects but also profound psychological consequences and an economic impact. It significantly compromises the quality of life of affected patients and increases the risk of developing depression and anxiety disorders [5, 6]. In 2002, the economic burden of endometriosis in the United States alone reached $22 billion [7].

Numerous theories have emerged in an attempt to unravel the pathogenesis of endometriosis. The widely embraced retrograde menstruation theory, proposed by Sampson, suggests the infiltration of endometrial tissue into the pelvic cavity during menstruation [3]. However, the occurrence of endometriosis in individuals without a uterus challenges the exclusive validity of this theory, pointing towards the involvement of alternative mechanisms [8]. Another hypothesis, known as coelomic metaplasia, postulates the transformation of mesothelial cells in the peritoneum, pleura and ovaries into endometrial-like tissue [9]. Despite these theories, the full complexity of endometriosis remains enigmatic, as neither these nor other proposed explanations such as angiogenic spread, lymphogenic spread, stem cells or Mullerian rests have provided comprehensive insights. Factors including genetic predisposition, epigenetic alterations, endocrine influences and aberrant immune responses are believed to contribute to the multifaceted development of endometriosis [10, 11].

Inflammation plays a crucial role in endometriosis, although it is not yet clear whether it initiates the disease or perpetuates it [1]. A concept of the possible role of infectious agents in initiating endometriosis has emerged [12, 13]. The "theory of contamination" or "infectious theory" suggests that microorganisms, along with endometrial tissue, can travel to the upper genital tract and peritoneal cavity during retrograde menstruation [14].

Recent research has highlighted the potential involvement of human papillomavirus (HPV) in endometriosis. HPV is a prevalent sexually transmitted infection, encompassing a wide spectrum of diseases, from low-risk types causing anogenital warts to high-risk types associated with anogenital and oropharyngeal cancers [15]. Interestingly, most patients infected with HPV do not exhibit discernible clinical signs or symptoms [16]. Consequently, the role of HPV in endometriosis has attracted attention in studies conducted over the past decade [17–20]. Building upon these considerations, the current study aims to systematically review the existing literature concerning this topic.

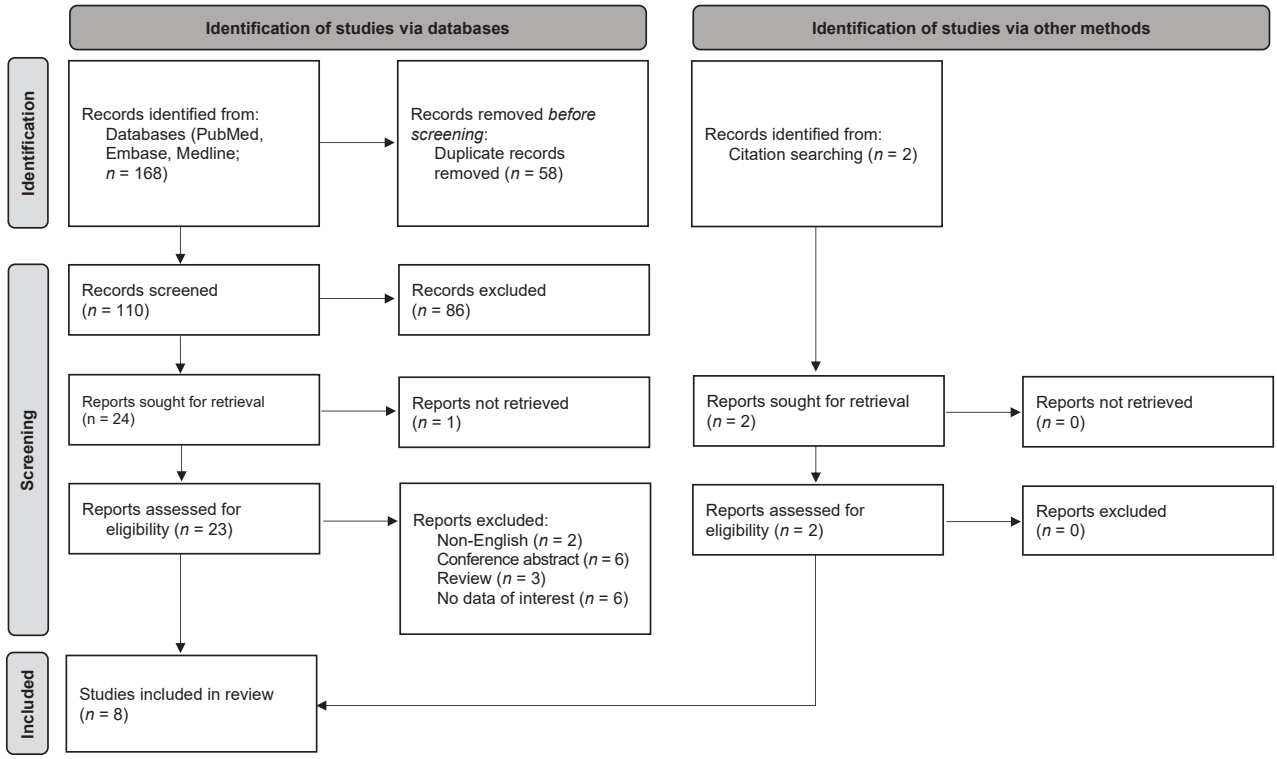

Figure 1. Flow diagram showing the search strategy, screening, eligibility and exclusion criteria

Methods

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were followed to conduct this systematic review. Two authors (A.S. and I.W.) conducted a comprehensive literature search of the online databases Embase, Medline and PubMed, using keywords: (endometrios*) OR (adenomyos*) AND (HPV) OR (human papillomavir*) OR (human papilloma vir*), as well as Medical Subject Headings (MeSH) terms. Our search was limited to English articles published from June 2013 to June 2023. Additionally, we performed a manual search of the reference lists of the review articles and identified two relevant citations outside of our accepted time frame, which we decided to include in our review. EndNote software was used to delete duplicate articles. Title and abstract screening were performed before obtaining the full text of eligible articles. A flow diagram of the systematic review is shown in Figure 1 (PRISMA template).

Results and discussion

Endometriosis is characterised as a chronic inflammatory disease that disrupts crucial immune processes. This results in inflammation and dysregulated immunomodulation, impairing the ability of immune-associated cells such as macrophages, neutrophils, dendritic cells, natural killer cells and mast cells to identify and eliminate ectopic endometrial tissue [21]. While there have been efforts to establish a single theory explaining the development of endometriosis, recent acceptance of its multifactorial pathogenesis has shifted the focus towards identifying specific factors that may predispose individuals to develop this disease.

HPV infection is widespread in the world's population and is one of the most common sexually transmitted diseases worldwide. Most sexually active adults will have an HPV infection at some point during their lives, although they may remain unaware, as it is typically asymptomatic and resolves spontaneously [22]. However, in some cases, persistent HPV infection can lead to neoplastic transformation, ultimately resulting in cancer development. This transformation is primarily driven by viral E6 and E7 oncoproteins, which exert an anti-apoptotic effect and promote cell immortalisation in infected cells [23].

Interestingly, similar mechanisms are recognised in the tissues of individuals with endometriosis. Endometriosis lesions demonstrate invasive biological features, including resistance to apoptosis and proangiogenic effects [24, 25]. Moreover, women with endometriosis have been found to be more susceptible to certain malignancies, such as ovarian cancer and non-Hodgkin's lymphoma [26]. This increased vulnerability may be attributed to shared characteristics of malignancy, such as local invasive growth and distant implantation.

Notably, the regulation of HPV genes has been demonstrated to be positively influenced by oestrogen, aligning with endometriosis being an oestrogen-dependent disease [27]. This link prompted researchers to investigate the potential correlation between HPV infection and the development of endometriosis, given the shared pathophysiological mechanisms and the high prevalence of both conditions in the population. The main characteristics of the studies included are summarised in Table 1.

In a case-control study conducted in Germany in 2010, Oppelt et al. aimed to investigate the hypothesis that viral infection of the endometrium, combined with retrograde menstruation and impaired immune response, might increase the likelihood of developing endometriotic lesions and their persistence in the peritoneal cavity or myometrium [20]. For this purpose, a total of 66 endometriosis lesions from 56 patients, which included peritoneal (n = 49), ovarian (n = 16) and endometrial (n = 1) lesions, were analysed. To detect HPV-DNA and other pathogens, polymerase chain reaction (PCR) amplification was performed, followed by a specific enzyme-linked immunosorbent assay (ELISA). The results were compared to 30 control tissues including endometrium (n = 14), peritoneum (n = 14), ovary (n = 1) and vagina (n = 1) from 13 patients with endometriosis (patient matched) and 13 patients without endometriosis.

Table 1. Studies investigating the association between HPV and endometriosis included in the current study

Authors and date	Type of study and country	Sample size and characteristics	Methods	Results
Oppelt et al. 2010 [20]	Case-control study (Germany)	70 patients; 66 endometriosis lesions from 56 patients (peritoneal *n* = 49, ovarian *n* = 16, endometrium *n* = 1) 30 control tissue samples (endometrium and peritoneum) from patient-matched (*n* = 13) and patients without endometriosis (*n* = 13)	• Surgical isolation of endometriotic lesions; histological diagnosis • HPV detection: tissue sample HPV-DNA PCR-based ELISA detection; subtype identification using Invader 2.0 HPV High-Risk Molecular Assay	• HPV was detected in 7 (11.3%) of 62 interpretable endometriosis samples from independent patients (71.4% hrHPV and 28.6% mrHPV) and in 8 (27.5%) of 29 control tissues (75% hrHPV and 25% mrHPV)
Vestergaard et al. 2010 [19]	Case-control study (Denmark)	32 patients; 32 and 27 eutopic endometrial and ectopic (ovarian or peritoneal) endometriosis samples, respectively, from the same group of patients; 20 endometrial samples from non-endometriosis patients; cervical swabs	• Surgical isolation of endometriotic lesions; histological diagnosis • HPV detection: cervical swab; tissue sample HPV PCR analysis and sequencing; further subtype identification by BLAST	• HPV was detected in 1 (*n* = 1/32; 3.1%) and 2 (*n* = 2/20; 10%) eutopic endometriotic and non-endometriotic samples, respectively (*p* = 0.62) • No HPV was detected in ectopic endometriotic samples (*n* = 0/25)
Heidarpour et al. 2017 [17]	Cross-sectional study (Iran)	99 patients; 50 and 49 ovarian samples with and without endometriosis, respectively	• Surgical isolation of endometriotic lesions; histological diagnosis • HPV detection: tissue sample HPV PCR analysis; subtype identification by HPV High-risk Typing PCR Kit	• hrHPV was detected in 13 (26%) and 5 (10.2%) of the samples with and without endometriosis, respectively (*p* = 0.041, χ^2 = 3.16)
Rocha et al. 2019 [18]	Case-control study (Brazil)	60 patients; 29 and 31 endometriosis and non-endometriosis tissue samples, respectively (endometrial tissue, pouch of Douglas fluid, uterine tube lavage and ovarian biopsy samples); cervicovaginal swabs	• Surgical isolation of endometriotic lesions; diagnosis • HPV detection: cervicovaginal swab; tissue sample HPV PCR analysis; HPV subtype identification by PCR-RFLP	• HPV was detected in 24 (*n* = 24/29; 82.8%) and 12 (*n* = 12/31; 38.7%) of the samples with and without endometriosis, respectively • Over 6-fold increased risk of infection in endometriosis patients (OR 6.64, 95% CI 2.00–22.04; *p* = 0.001) • Increased risk of hrHPV infection in LGT and in UGT in endometriosis patients (respectively, OR 8.5, 95% CI 2.50–28.70; *p* = 0.0002 and OR 3.6, 95% CI 1.09–12.30; *p* = 0.03)
Matalliotakis et al. 2021 [28]	Retrospective, epidemiological and noncomparative study (Greece)	Clinical, surgical, and pathological records from 860 women (1990–2020) with endometriosis undergoing gynaecological surgical treatment; 27 patients with histologically confirmed cervical endometriosis	• N/A	• HPV was detected in 16 (*n* = 16/27; 59.2%) samples with cervical endometriosis (*p* < 0.05)
Hong et al. 2023 [33]	Cross-sectional study (US)	129 patients with endometriosis; cervicovaginal swabs	• Self-report of physician-diagnosed endometriosis collected via health questionnaire • HPV detection: cervicovaginal swab genotyping	• HPV and hrHPV was diagnosed in 57 (*n* = 57/129; 36.9%; *p* = 0.35) and 31 (*n* = 31/129; 19.8%; *p* = 0.15) patients with endometriosis, respectively • No significant association was found between the prevalence of hrHPV and the diagnosis of endometriosis (aPR 0.71, 95% CI 0.44–1.14) • Prevalence of HPV in women with endometriosis was higher in participants with health insurance than those without (respectively, aPR 1.44, 95% CI 0.94–2.20 and aPR 0.71, 95% CI 0.50–1.03; *p* = 0.01)

Table 1. Studies investigating the association between HPV and endometriosis included in the current study

Authors and date	Type of study and country	Sample size and characteristics	Methods	Results
Moslehi et al. 2023 [30]	Cross-sectional study (Iran)	81 endometriotic tissue samples (endometrial tissue, pouch of Douglas fluid, utero-sacral ligament, bladder, rectal and ovarian biopsy samples); exocervical swabs	• Surgical isolation of endometriotic lesions; clinical or histological diagnosis • HPV detection: exocervical swab; tissue biopsy sample analysis by HPV Direct Flow CHIP and PCR	• HPV was detected in 20 (n = 20/81; 24.69%) patients (9 women with pelvic HPV, 9 women with vaginal HPV, and 2 women with both)
Zullo et al. 2023 [32]	Observational, prospective, cohort study	457 patients; cervical swabs; endometrial and granulosa cell samples collected before or during IVF procedure	• Endometriosis diagnostic criteria not stated • HPV detection: cervical, endometrial and granulosa cells HPV PCR-based detection	• Endometriosis was significantly more frequent in hrHPV-positive than in negative women (31.6% vs 10.1%; $p < 0.01$)

HPV – human papillomavirus; hrHPV – high-risk HPV; mrHPV – medium-risk HPV; OR – odds ratio; CI – confidence interval; aRP – adjusted prevalence ratio; US – United States; BLAST – Basic Local Alignment Search Tool; PCR – Polymerase Chain Reaction; PCR-RFLP – Polymerase Chain Reaction-Restriction Fragment Length Polymorphism; LGT – lower genital tract; UGT – upper genital tract.

The study's results showed that 6% of lesions in the study group and 3.3% in the control group were non-interpretable. Among the interpretable lesions, 88.7% in the study group and 72.4% in the control group tested negative for HPV-DNA. Interestingly, 7 out of 62 interpretable endometriosis lesions from independent patients (11.3%) tested positive for HPV-DNA. Among these positive cases, 71.4% were classified as high-risk subtypes, and 28.6% as medium-risk subtypes. In the control group, 8 out of 29 interpretable control tissues (27.5%) were also found to be HPV positive. Among these cases, 75% were classified as high-risk subtypes, while 25% were medium-risk subtypes. Notably, 1 patient in this group had an HPV 18-positive ovarian endometriosis lesion, which was also associated with an ovarian adenocarcinoma in the same ovary, indicating a possible endometriosis-associated carcinoma. This finding raised significant interest. Moreover, a paraffin tissue section from the remaining normal ovary of this patient was tested for HPV-DNA using immunohistochemistry, and surprisingly, it was found to be HPV-negative, contrasting with the HPV-positive ovarian lesion. Despite these observations, the authors concluded that due to the limited testing of study participants for HPV-DNA, it remains challenging to definitively ascertain whether persistent HPV infection increases the risk of endometriosis. To gain more conclusive insights, further research involving a larger number of patients specifically tested for HPV-DNA would be required. Nevertheless, the study's findings suggest that persistent HPV infection, particularly involving high-risk types, within an endometriosis lesion may potentially play a role in promoting its transformation into a carcinoma.

In a study conducted in Denmark by Vestergaard et al., they investigated the potential involvement of pathogenic viruses, including HPV, in 52 Danish patients with and without endometriosis using highly sensitive PCR tests [19]. Samples were collected from the eutopic endometrium of all 32 women suffering from endometriosis, and in addition, ectopic endometriotic lesions were obtained from 27 of these patients through excision with scissors or biopsy forceps. The ectopic tissue was sourced from either one of the ovaries or the peritoneum. 20 women with no indication of endometriosis were included as healthy controls. In this study, 3 cases with positive HPV were detected. Among the 32 endometriosis patients, only 1 sample (3%) tested positive for HPV-DNA, while HPV was detected in the endometrium of 2 women in the control group (10%). The prevalence of HPV-DNA did not display a significant difference between the 2 study groups. Interestingly, no HPV was found in the samples obtained from the ectopic group. Considering these findings, the authors concluded that the prevalence of pathogenic DNA viruses, including HPV, in the endometrium and endometriosis lesions is remarkably low. Consequently, this finding does not strongly support the hypothesis of a viral pathophysiology of endometriosis. Nevertheless, they underscored that the possibility of an infectious causal agent cannot be entirely ruled out based on the presented results. Therefore, further investigations in this area are warranted to gain a more comprehensive understanding of any potential association between viral infections and the development of endometriosis.

In 2017, Heidarpour et al. conducted a cross-sectional study in Iran to delve further into the topic, as previous literature presented inconclusive results [17]. The study involved 99 patients, with 50 samples of ovarian endometriosis and 49 samples of ovarian tissue from women without endometriosis. The researchers utilised PCR to assess the prevalence of high-risk human papillomavirus (hrHPV) in these samples. Notably, there were no significant differences between the groups concerning age, marital status or parity. The study's findings revealed a noteworthy result: the prevalence of high-risk HPV was significantly higher in patients with endometriosis, with 13 cases (26%) compared to 5 cases (10.2%) in patients without endometriosis. However, the study did have certain limitations, including a retrospective design and a lack of access to more detailed data about the studied patients. Additionally, the sample size was relatively small. Despite these limitations, the authors emphasised the necessity for further prospective research on larger groups of patients, accompanied by thorough clinical analysis. During laparoscopic surgery, researchers collected samples from both the upper genital tract (UGT) and lower genital tract (LGT) of the participants and analysed them using PCR to detect the presence of HPV and 7 other sexually transmitted infections (STIs). Initially, the participants were divided into 2 groups: infertile patients (n = 25) and fertile controls (n = 35). After analysing the surgical findings, they further divided the participants into an endometriosis group (n = 29) and a non-endometriosis control group (n = 31). Among the 60 women studied, 36 (60%) tested positive for 13 different HPV types in either the LGT, UGT or both. Out of these cases, 7 (53.8%) were low-risk (lr) HPV, and 6 (46.2%) were high-risk (hr) HPV. Among the HPV-DNA-positive women, 25 (69.4%) had only hrHPV, 7 (19.4%) had only low risk HPV (lrHPV), and 4 (11.1%) had multiple HPV infections.

Regarding the infertile patients, 15 out of 25 (60%) had HPV-DNA, with 13 of them (87%) having hrHPV. Statistically, when comparing UGT sites, infertile patients were significantly more often hrHPV positive compared to the fertile control group, with an over three-fold increased risk. Interestingly, only hrHPV types were detected in the UGT for both infertile patients and fertile controls.

In relation to endometriosis patients, 24 out of 29 (82.8%) were HPV-DNA positive, whereas in the non-endometriosis control group, HPV-DNA was detected only in 12 out of 31 (38.7%) cases, resulting in an increased risk of infection higher than six-fold for the endometriosis patients. Furthermore, in patients with endometriosis, hrHPV was present both in the LGT and UGT sites, with an over eight-fold increased risk for the former and over three-fold increased risk for the latter. Similarly to the previous cases, only hrHPV types were detected in the UGT, regardless of the group. This study marked the first time that a continuum of hrHPV infection was observed from the LGT to the UGT. Additionally, it revealed an association between hrHPV infection in the UGT with infertility, particularly with endometriosis. Interestingly, no association with either endometriosis or infertility was observed among the other 7 STIs studied. Moreover, the study found that only infertile and endometriosis patients had hrHPV detected in the ovaries, while their respective control groups did not show such findings.

This topic has continued to captivate scientists in recent years. In 2021, Matalliotakis et al. published a retrospective, epidemiological and noncomparative study focusing on cervical endometriosis [28]. Among 860 records of women with endometriosis who underwent surgical treatment, 27 were diagnosed with cervical endometriosis based on tissue biopsy. Through retrospective analysis of these 27 cases, a compelling relationship between cervical endometriosis and cervical intraepithelial neoplasia (CIN) emerged, with 19 out of 27 cases (70%) showing a coexistence with CIN. Furthermore, the study confirmed a high prevalence of HPV in this group, as HPV was detected in 16 out of 27 samples with cervical endometriosis (59.2%). The study also revealed the coexistence of malignant gynaecological pathologies in 7 cases, comprising 2 with cervical cancer (7.4%), 2 with endometrial cancer (7.4%) and 3 with ovarian cancer (11.1%). However, it is important to note that the focus of interest in this study was not solely on the presence of HPV-DNA but rather the cervical dysplasia resulting from it and the role of a coexistence between this pathology and cervical endometriosis. Based on the results, the authors concluded that while the pathophysiology and genetics of cervical dysplasia are well defined, further research is necessary to establish a robust association between cervical endometriosis and gynaecological premalignant and malignant pathology. The findings highlight the importance of continued investigation to gain a more comprehensive understanding of the intricate relationship between cervical endometriosis, HPV infection and the development of gynaecological malignancies.

In 2023, Hong et al. conducted the first national representative survey in the United States to investigate the prevalence of genital human papillomavirus (HPV) in women with endometriosis [29]. The study included 1,768 women, providing insights into a broader population of females. Data was collected between 2003 and 2006, a period preceding the approval of an HPV vaccination by the US Food and Drug Administration (FDA). Among the study participants, 129 women reported physician-diagnosed endometriosis, accounting for 9.5% (95% CI 7.3–12.3) of the group. HPV and hrHPV were diagnosed in 57 (36.9%) and 31 (19.8%) patients with endometriosis, respectively. Despite these findings, the study did not reveal a significant association between the prevalence of high-risk HPV and the diagnosis of endometriosis, even after accounting for multiple sociodemographic factors. Interestingly, the authors also observed that the association between endometriosis and HPV infection varied depending on access to health care. For participants without health insurance coverage, the prevalence of any HPV infection in women with endometriosis was higher than in those without endometriosis. Conversely, in a subgroup with health insurance, a statistically significant lower prevalence of any HPV infection was observed in women with endometriosis.

In 2023, another noteworthy cross-sectional study was conducted by Moslehi et al. in Iran, involving 81 women who underwent laparoscopic surgery for endometriosis [30]. Among these participants, 20 women (24.69%) were found to be infected with HPV, with low-risk HPV being more prevalent in the study population. Interestingly, the study results showed that HPV infection was not significantly associated with the severity of endometriosis, age, BMI, parity, disease duration since diagnosis, uterus size, history of surgery, urinary signs, menstrual status or treatment method. When considering the prevalence of HPV infection in the Iranian population, which is estimated to be between 7–10%, it is evident that HPV is more common among patients with confirmed endometriosis (24.69%) compared to the general population [31].

In 2023, a recent observational, prospective cohort study conducted by Zullo et al. presented different conclusions compared to the two previous publications of that year [32]. The study aimed to assess the prevalence of HPV infection in women undergoing in vitro fertilisation (IVF) and its potential effects on embryonic development and IVF outcomes. A total of 457 women with couple's infertility, who were candidates for IVF, underwent HR-HPV testing. Out of these participants, 326 underwent their first IVF cycle and were included in the analysis. Among them, 41 (8.9%) were found to be HPV positive based on cervical swab tests. The study found that HPV prevalence was higher in younger women and decreased linearly with age. An interesting observation was that among the various causes of infertility, endometriosis stood out as being significantly more frequent in hrHPV-positive women than in hrHPV-negative women (31.6% vs 10.1%). However, no significant difference was observed in the distribution of other causes of infertility between couples with HPV-positive or negative cervical swabs.

Similar to the findings presented by Rocha et al., this study supported the observation that HPV can move along the female genital tract and infect the upper genital tract (UGT) in a considerable proportion of women who test positive for HPV at the cervical level. Additionally, the authors suggested that the hypothesis of an active involvement of HPV in the development of endometriosis warrants further investigation. The potential oncogenic effect of HPV at the endometrial and ovarian levels, as discussed in the study by Oppelt et al., also requires further scrutiny.

Considering the aforementioned studies, it is essential to note the heterogeneity of the presented results, which may be attributed to the diversified research methodologies, the relatively small size of the study groups and the primarily retrospective nature of the research. Out of the 8 reviewed papers, 3 demonstrated a statistically significant correlation between HPV infection and endometriosis, while three others indicated a higher incidence of HPV infection in patients with confirmed endometriosis, although a significant correlation was not conclusively established due to the limitations of the research methodologies and sample sizes. Heidarpour et al., Oppelt et al., Rocha et al., Matalliotakis et al., Moslehi et al. and Zullo et al. reported higher rates of HPV detection in endometriosis lesions, contrasting with Vestergaard et al. and Hong et al., whose studies did not find such a correlation [17–20, 28–30, 32]. Furthermore, a difference was observed in the dominant type of HPV serotype in the study populations. Heidarpour et al. and Rocha et al. found that hrHPV was most common among patients diagnosed with endometriosis, whereas Moleshi et al. showed that lrHPV was more prevalent.

Based on the presented literature review, it is currently challenging to scientifically substantiate the hypothesis of a viral origin of endometriosis. In none of the studies was a causal relationship between the presence of HPV-DNA and endometriosis demonstrated. Based on the available data, it cannot be ruled out that there is another factor contributing to the presence of both.

However, it is noteworthy that there are some studies which suggest that persistent HPV infection of the female genital tract,

particularly with hrHPV, may predispose the invasive capacity of endometrial tissue, leading to the formation of endometrial lesions as a possible effect of retrograde menstruation [32].

All cited authors agree that further research should be conducted to delve deeper into this matter and determine the potential role of HPV infection in the formation of endometrial lesions. To establish a more comprehensive understanding, larger and more well-designed studies are required, incorporating prospective methodologies and considering potential confounding factors. Until then, the exact relationship between HPV and endometriosis remains an intriguing area for ongoing investigation.

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