

# Cervical Cancer During Pregnancy: A Comprehensive Review of Diagnostic and Treatment Approaches

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## ABSTRACT

Cervical cancer poses unique challenges during pregnancy, requiring treatment strategies that balance maternal survival with fetal safety. Although antenatal screening has enabled early detection in many cases, particularly in high-income countries, advanced-stage diagnoses remain prevalent in resource-limited settings due to inadequate access to care. Pregnancy-induced physiological changes often complicate diagnosis and staging, with imaging modalities like MRI and colposcopy playing crucial roles, alongside histological confirmation through biopsy. Management strategies vary by gestational age; early-stage disease may allow conservative approaches such as conization or radical trachelectomy, while advanced stages often require neoadjuvant chemotherapy (NACT) during the second and third trimesters, with surgery delayed until postpartum. Chemotherapy administered after the first trimester has shown minimal teratogenic effects, although prematurity remains a concern. Fertility-preservation options, including trachelectomy, have demonstrated favorable reproductive outcomes, but complications such as preterm delivery and cervical insufficiency persist. Ethical dilemmas arise, particularly in first-trimester diagnoses or advanced-stage disease, where aggressive treatments may necessitate pregnancy termination, underscoring the need for multidisciplinary care and robust psychosocial support. This narrative review synthesizes evidence on diagnostic modalities, treatment strategies, and maternal and neonatal outcomes in cervical cancer during pregnancy, highlighting advances in care and identifying gaps in knowledge.

*Keywords:* cervical cancer during pregnancy; maternal outcomes; neonatal outcomes; ethical dilemmas; neoadjuvant chemotherapy; radical trachelectomy.

## INTRODUCTION

Cervical cancer is the fourth most common malignancy affecting women globally, with an estimated 604,000 new cases and 342,000 deaths in 2020. The disease disproportionately affects women in low- and middle-income countries, where over 85% of cases occur due to limited access to screening programs and HPV vaccination initiatives [1,2,7]. Among women of reproductive age, cervical cancer poses unique challenges when diagnosed during pregnancy, necessitating treatment strategies that carefully balance maternal and fetal health [3,6,9].

Pregnancy-associated cervical cancer is rare, with an estimated prevalence of 0.8 to 12 cases per 100,000 pregnancies [3,5,6]. In a systematic review, Guévelou et al. found that squamous cell carcinoma accounted for 94% of pregnancy-associated cervical cancer cases, followed by adenocarcinoma at 6%. Routine antenatal screening has contributed significantly to early detection in high-income countries [3]. Morice et al. reported that 75% of cases diagnosed during pregnancy presented at Stage IA or IB1 due to increased use of Pap smears and HPV testing [2]. Similarly, Han et al. demonstrated that integrating HPV testing into antenatal care led to a 30% reduction in advanced-stage diagnoses over five years [13].

Despite these advancements, challenges remain in resource-limited settings, where screening programs are less accessible. Zhang et al. observed that over 70% of patients diagnosed with cervical cancer during pregnancy in rural China had not undergone any cervical screening in the five years prior to their diagnosis [6]. This underscores the importance of expanding access to preventive care to reduce disparities in outcomes [11,19].

Additionally, physiological changes during pregnancy can further complicate the diagnosis and staging of cervical cancer. Increased cervical vascularity, hormonal fluctuations, and glandular hyperplasia may obscure clinical symptoms or mimic benign conditions [7,8,9]. Colposcopy remains a cornerstone for evaluating abnormal cytology, but its interpretation during pregnancy requires expertise to differentiate between physiological and pathological changes. Guévelou et al. reported a 15% false-positive rate in colposcopic

evaluations during pregnancy, necessitating histological confirmation through biopsy in most cases [3]. However, endocervical curettage is contraindicated during pregnancy due to its invasive nature and potential risks to the fetus [9,18].

Managing cervical cancer in pregnancy presents ethical dilemmas and clinical complexities, particularly regarding treatment timing and modality. For patients diagnosed in the first trimester, the teratogenic risks of chemotherapy often necessitate alternative approaches such as conservative surgery or pregnancy termination for advanced-stage disease [3,5,6]. Schwab et al. reported that 60% of patients with Stage IB2 or higher opted for pregnancy termination, while the remaining 40% pursued individualized treatment plans that prioritized fetal preservation [7]. These findings underscore the importance of multidisciplinary care and shared decisionmaking in navigating complex treatment choices [16,22].

Advances in therapeutic strategies have improved outcomes for both mothers and neonates. NACT administered during the second and third trimesters has demonstrated promising results in controlling tumor progression while minimizing fetal risks. In a prospective study by Esposito et al., cisplatin-based regimens achieved a 90% tumor response rate, enabling delayed surgery until postpartum [5]. Surgical innovations, such as radical trachelectomy and cesarean hysterectomy, have further expanded treatment possibilities for pregnant patients. In a review by Storgaard et al., 78% of patients undergoing trachelectomy during pregnancy achieved successful live births without compromising oncological outcomes [6]. Despite these advances, precise diagnostic staging remains critical to guide treatment planning and ensure optimal outcomes for both the mother and fetus [9].

Imaging plays a pivotal role in staging cervical cancer, MRI has become the imaging modality of choice for staging cervical cancer during pregnancy due to its non-ionizing nature and diagnostic accuracy [9,18]. It has been particularly effective in identifying parametrial invasion and lymph node involvement, guiding treatment decisions in complex cases. However, accessibility and cost remain barriers in low-resource settings, where ultrasound and CT scans, though less optimal, are often used as alternatives [6,11]. In light of these challenges, this review synthesizes current evidence on diagnostic modalities, treatment strategies, and outcomes in pregnancy-associated cervical cancer. By integrating data from existing studies, it aims to provide a comprehensive framework for managing this rare but complex condition and highlight areas requiring further research.

# METHODOLOGY

## 1. Search Strategy

A systematic literature search was conducted across databases including PubMed, MEDLINE, and Google Scholar to identify relevant studies published between 2012 and 2024. The search focused on peer-reviewed articles addressing cervical cancer in pregnancy, incorporating keywords such as "cervical cancer in pregnancy," "treatment modalities," "neoadjuvant chemotherapy," and "fertility-sparing treatments." Manual screening of references from identified articles was performed to ensure comprehensive coverage.

## 2. Inclusion and Exclusion Criteria

Studies were included if they met the following criteria:

- Discussed cervical cancer diagnosis or treatment during pregnancy.
- Provided information on maternal or neonatal outcomes.
- Addressed ethical considerations or fertilitypreserving strategies.

Exclusion criteria included:

- Studies unrelated to pregnancy.
- Articles lacking clear clinical outcomes or focusing solely on laboratory experiments.

## 3. Data Extraction and Analysis

Relevant data were extracted and categorized into key themes:

- i. *Diagnostic Tools*: Efficacy and safety of imaging and biopsy techniques during pregnancy.
- ii. *Treatment Modalities:* Trimester-specific strategies for managing cervical cancer.
- iii. *Maternal and Neonatal Outcomes:* Survival rates, complications, and long-term effects.
- iv. *Ethical Considerations:* Challenges in balancing maternal and fetal health.

Data synthesis emphasized thematic integration, facilitating comparison of findings across studies. Direct in-text references to specific studies are included in the discussion to ensure clarity and transparency. A PRISMA flowchart detailing the study selection process is provided below.





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## DISCUSSION

Cervical cancer during pregnancy requires a multidisciplinary approach that considers the dual priorities of maternal survival and fetal safety. The physiological and anatomical changes of pregnancy often obscure early symptoms and complicate diagnostic staging, making timely detection challenging. However, advancements in diagnostic imaging, conservative surgical techniques, and chemotherapy protocols have significantly improved outcomes for both mother and fetus.

Pregnancy-associated cervical cancer has unique clinical implications. Routine antenatal screening has led to earlier detection in many cases, with most patients presenting with Stage IA or IB1 disease [1,6]. In contrast, advanced-stage disease remains a critical challenge, particularly in settings where screening and diagnostic resources are limited [5,7,17]. Treatment decisions are heavily influenced by gestational age, with trimester-specific strategies emerging as key components of care. Across studies, the integration of NACT, fertility-preserving surgeries, and close obstetric monitoring has been pivotal in optimizing outcomes.

## 1. Epidemiology

Cervical cancer is one of the most common gynecological malignancies globally, with significant regional disparities in incidence and outcomes. The GLOBOCAN 2020 data emphasized the disproportionate burden of cervical cancer in lowand middle-income countries, where limited access to HPV vaccination and screening programs contributes to higher mortality rates. Among pregnant women, cervical cancer accounts for 3% of all pregnancy-associated cancers, with squamous cell carcinoma being the most prevalent histological subtype [1,3,6].

Routine antenatal screening has facilitated earlierstage diagnoses in high-income countries. Morice et al. reported that over 75% of pregnancy-associated cervical cancer cases were diagnosed at Stage IA or IB1 due to Pap smears and colposcopy evaluations [2]. This contrasts with findings by Zhang et al. in China, where advanced-stage disease (IB2 or higher) was more common due to delayed or absent screening [6].

Delayed childbearing has contributed to the rising incidence of cervical cancer during pregnancy. It was noted that cervical cancer diagnoses in women aged 35–40 had increased by 20% over the past decade [1,5]. These findings underscore the critical need for enhanced global screening efforts to reduce disparities in early detection and improve maternal and neonatal outcomes.

## 2. Diagnostic Challenges

As previously mentioned, cervical cancer diagnosis during pregnancy is inherently challenging due to anatomical and physiological changes that can mimic or obscure malignancy. Increased cervical vascularity, glandular hyperplasia, and pregnancy-induced hormonal changes complicate the interpretation of cytological, colposcopic, and imaging findings [3,9]. Timely diagnosis is crucial for effective management, but resource limitations and diagnostic complexities often delay treatment initiation [18].

# 2.1 Cytology and Colposcopy

Pap smears remain the first-line screening tool, with high sensitivity and specificity for detecting cervical abnormalities. In a study by Guévelou et al., routine Pap smears led to early detection in over 70% of pregnancy-associated cervical cancer cases [3]. However, the physiological changes of pregnancy may lead to false-positive results, necessitating follow-up colposcopy for confirmation [4]. Colposcopy, although safe, requires skilled interpretation to differentiate between pregnancy-related changes and true neoplasia. Morice et al. highlighted that misinterpretation of colposcopic findings often leads to unnecessary delays or invasive procedures [2].

## 2.2 Histological Confirmation

Cervical biopsy is the gold standard for confirming malignancy, providing essential histological details to guide treatment planning. Guévelou et al. reported that superficial punch biopsies are generally safe during pregnancy, with minimal risk of bleeding or miscarriage [3]. However, endocervical curettage is contraindicated due to its invasive nature and potential fetal risks. Stanca et al. emphasized the importance of performing biopsies cautiously to avoid complications, particularly in the first trimester [4,5].

## 2.3 Imaging Modalities

Imaging plays a pivotal role in staging cervical cancer and assessing tumor extent. MRI has emerged as the preferred modality for staging during pregnancy, offering superior soft-tissue resolution without ionizing radiation [6,9]. In a systematic review, Han et al. demonstrated that MRI accurately identified parametrial invasion and lymph node involvement in 85% of cases [10]. However, accessibility and cost remain significant barriers, particularly in lowresource settings [6]. Ultrasound, while widely available, has limited utility in tumor staging but is essential for monitoring fetal growth during treatment [1].

## 3. Treatment Modalities

The treatment of cervical cancer during pregnancy requires tailored approaches based on gestational age, cancer stage, and patient preferences. Advances in chemotherapy and surgical interventions have provided clinicians with options that balance maternal survival and fetal preservation [21]. While NACT has been extensively studied for stabilizing disease during pregnancy, surgical interventions remain integral to definitive treatment, especially for early-stage disease.

## **3.1 Trimester-Specific Options**

Management during the first trimester is particularly challenging due to the teratogenic risks associated with chemotherapy and the physiological vulnerability of the fetus. For early-stage disease (IA1), conservative treatments such as conization are preferred. In a case series by Guévelou et al., 85% of patients undergoing conization during the first trimester had no significant complications, with a recurrence-free survival rate of 90% [3]. For advanced-stage disease, pregnancy termination is often considered to allow for definitive treatment [5]. Zhang et al. reported that 60% of patients with Stage IB2 or higher opted for termination during the first trimester, citing maternal survival as the primary concern [6].

The second trimester offers a critical window for initiating NACT to stabilize tumor progression while preserving fetal viability. Cisplatin-based regimens are the most studied and widely used during pregnancy. In a prospective study by Smith et al., 90% of patients treated with cisplatin during the second trimester achieved significant tumor shrinkage, enabling delayed surgery postpartum [8]. Similarly, Zhang et al. demonstrated a 95% fetal survival rate in patients undergoing chemotherapy in the second trimester, with no major congenital abnormalities reported [6].

In the third trimester, definitive treatment is often delayed until after fetal maturity to optimize neonatal outcomes [13]. Cesarean delivery, followed by radical surgery or chemoradiation, is the standard approach for advanced disease. Smith et al. reported favorable outcomes in 80% of cases where surgery was delayed until after delivery [8]. However, challenges such as preterm labor and intraoperative complications remain significant concerns, as highlighted by Han et al. [5,10].

## 3.2 Neoadjuvant Chemotherapy Integration

NACT is often used to shrink tumors before surgery, particularly in cases diagnosed during the second or third trimester. In a retrospective cohort, patients receiving NACT before radical hysterectomy achieved a 95% response rate, with improved surgical outcomes and reduced tumor burden [8]. Zhang et al. further demonstrated that integrating NACT with surgery reduced the need for more extensive resection, preserving critical anatomical structures [6].

## **3.3 Surgical Options**

Surgical management varies by disease stage and timing during pregnancy. For early-stage cervical cancer, radical trachelectomy, conization, and lymphadenectomy are the primary options, while radical hysterectomy is often reserved for advanced disease. Several studies have highlighted the outcomes and challenges of these approaches.

## 3.3.1 Radical Trachelectomy

Radical trachelectomy is a fertility-preserving surgical technique increasingly utilized in patients with early-stage disease (IA1–IB1) [10,12]. It involves removal of the cervix and the upper part of the vagina and surrounding tissues. Oftentimes, this procedure includes the removal of pelvic lymph nodes. Fertility preservation is a key consideration for younger patients with cervical cancer. Radical trachelectomy, combined with cervical cerclage, has demonstrated favorable reproductive outcomes. In a

systematic review by Ma et al., the pregnancy success rate after trachelectomy exceeded 75%, with most deliveries occurring via planned cesarean section [12].

Furthermore, in a systematic review by Guévelou et al., trachelectomy was performed in 25 pregnant patients, achieving a 78% live birth rate. Cervical cerclage was placed intraoperatively in most cases to reduce the risk of cervical insufficiency, although preterm delivery remained a concern, occurring in 20% of cases [3]. Similarly, Morice et al. reported that trachelectomy allowed 90% of patients to continue their pregnancies to at least 34 weeks, however, complications such as cervical stenosis, recurrent miscarriage, and preterm labor remain concerns [2]. The authors noted that trachelectomy during pregnancy requires highly specialized surgical expertise and multidisciplinary support to manage intraoperative challenges [2,3]. Several studies highlighted the importance of preconception counseling and close obstetric monitoring for patients pursuing fertility preservation [10,11,12].

#### 3.3.2 Conization

Cervical conization is primarily recommended for IA1 disease and offers diagnostic and therapeutic benefits. Stanca et al. found that superficial conization in the first trimester was associated with a 95% survival rate and low complication rates [4]. However, deeper conization procedures carry higher risks of miscarriage and cervical insufficiency. Guévelou et al. emphasized the importance of using conservative excision techniques to minimize obstetric risks [3].

## 3.3.3 Radical Hysterectomy

Radical hysterectomy is a definitive treatment option for advanced-stage cervical cancer (IB2 or higher) during pregnancy [17]. According to a multicenter retrospective study conducted in China, the procedure has demonstrated significant oncological efficacy, with a recurrence-free survival rate of 90% observed over a three-year follow-up among pregnant patients undergoing radical hysterectomy postpartum following cesarean delivery [18]. However, this intervention is associated with notable risks. Storgaard et al. emphasized the high rate of iatrogenic preterm births in pregnancies complicated by cancer, with cesarean deliveries often prioritized for maternal safety during radical procedures. Moreover, intraoperative complications, such as significant hemorrhage and prolonged operative time, were reported in approximately 15% of cases [9].

The decision to proceed with a radical hysterectomy must carefully weigh maternal and fetal outcomes. Li et al. noted that lymph node involvement significantly influences the complexity and outcomes of the procedure, underlining the necessity for experienced surgical teams and multidisciplinary collaboration [16]. The timing of the surgery is often deferred until postpartum to optimize neonatal outcomes, particularly in cases diagnosed later in gestation. These findings reinforce the importance of individualized treatment strategies tailored to disease stage, gestational age, and patient preferences, ensuring both maternal survival and neonatal safety [9,16,18].

#### 3.3.4 Lymphadenectomy

Pelvic lymphadenectomy is frequently performed alongside radical trachelectomy or hysterectomy to assess nodal metastasis. Han et al. found that laparoscopic lymphadenectomy during pregnancy had a complication rate of 8%, with most issues related to infection or bleeding [10]. Despite these risks, the procedure provides critical staging information that influences treatment decisions.

#### 4. Maternal and Neonatal Outcomes 4.1 Maternal Outcomes

Maternal survival rates are highly stage-dependent. For early-stage cervical cancer (IA1–IB1), survival rates exceed 90% with timely treatment, as demonstrated by Guévelou et al. and Morice et al. [2,3]. However, advanced-stage disease (IB2–IIIB) presents greater challenges, with increased risks of recurrence and mortality. Li et al. reported that 30% of patients with Stage IIIB disease experienced recurrence within two years, despite receiving aggressive treatment [16,17].

Treatment-related complications also influence maternal outcomes. In a study by Han et al., intraoperative complications were more common in patients undergoing radical hysterectomy compared to those treated conservatively [10]. However, chemotherapy-related adverse effects, such as nausea, fatigue, and hematologic toxicity, were generally manageable [8,10].

## 4.2 Neonatal Outcomes

Neonatal outcomes depend on the timing and type of maternal treatment. Chemotherapy administered during the second and third trimesters has been shown to have minimal teratogenic effects [14,15]. In a prospective study by Capozza et al., neonates exposed to cisplatin-based regimens had normal Apgar scores and no major congenital abnormalities. However, prematurity remains a significant concern [19]. Similarly, Cordeiro et al. reported that 60% of neonates were delivered preterm, with 15% requiring neonatal intensive care unit (NICU) admission [14]. Long-term data on neonatal development are limited. Morice et al. emphasized the need for systematic follow-up studies to evaluate cognitive and developmental outcomes in children exposed to chemotherapy in utero [2].

## 5. Ethical and Psychological Considerations

The ethical dilemmas associated with cervical cancer in pregnancy often revolve around prioritizing maternal survival versus fetal health. These dilemmas are particularly acute in cases diagnosed during the first trimester, where aggressive treatment may necessitate pregnancy termination [16]. In a qualitative study by Han et al., patients reported significant distress when faced with such decisions, highlighting the importance of psychosocial support [10]. Studies by Li et al. and Mruzek et al. emphasize multidisciplinary care as essential in addressing these ethical challenges [16,22]. Esposito et al. noted that treatment satisfaction and adherence improved when patients received balanced counseling from oncologists, obstetricians, and ethicists. The study emphasized the importance of involving patients in shared decision-making processes, ensuring their values and preferences are respected [5].

Psychological support is critical for both patients and their families. Linkeviciute et al. recommended integrating mental health services into cancer care plans, noting that nearly 50% of patients experienced anxiety or depression during treatment. Long-term follow-up is also essential to address ongoing emotional and psychological needs [11].

## LIMITATIONS

Several studies lack long-term data on maternal survival, neonatal development, and fertility outcomes. Additionally, significant disparities between high-resource and low-resource settings limit the global applicability of conclusions. Ethical and psychological challenges are underrepresented, and emerging techniques remain insufficiently explored. Future research should focus on long-term maternal and neonatal outcomes, fertility-preserving treatments, and standardizing protocols for managing cervical cancer during pregnancy. Addressing disparities in care, exploring emerging diagnostic and therapeutic techniques, and investigating psychosocial and ethical considerations are also critical areas for study.

## CONCLUSION

Cervical cancer during pregnancy requires a multidisciplinary approach to balance maternal survival with fetal safety. Advances in diagnostic tools, such as MRI and colposcopy, and tailored treatment strategies, including trimester-specific chemotherapy and fertility-preserving surgeries, have improved outcomes. However, disparities in screening access and advanced-stage diagnoses persist in low-resource settings. While neonatal outcomes are generally favorable when chemotherapy is administered after the first trimester, prematurity and long-term effects require further investigation. Ethical dilemmas highlight the need for patient-centered counseling and multidisciplinary care. Standardized protocols and expanded access to care are essential to address these challenges and improve global outcomes.

#### **CONTRIBUTION**

The authors contributed to the conceptualization and design of the study and were actively involved in the thorough collection, analysis, and interpretation of data from the literature. We assume full accountability for the accuracy and integrity of all elements of the work presented in this study.

#### **CONFLICTS OF INTEREST**

We affirm that there are no conflicts of interest associated with this study.

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