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Cervical and Vaginal Deciduosis: Insights on Management and a Systematic Review of Observational Studies on Pregnancy Complications and Management Outcomes (Including Vaginal Birth)

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Abstract

Introduction. Deciduosis is an ectopic transformation of connective tissue into decidual-like cells. This is the first systematic review describing the clinical course, associated pregnancy complications, and management outcomes of cervical and vaginal deciduosis.

Methods. Our search covered worldwide observational studies published in English in five databases (PubMed, PubMed Central (PMC), Europe PMC, ScienceDirect, and Google Scholar) from inception to February 24, 2023. We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines and critically appraised studies using CAsE REport (CARE) and Joanna Briggs Institute (JBI) tools. Then, we extracted patient characteristics, clinical features, management-related information, and outcomes.

Results. The selection process identified 15 studies describing 30 pregnancies. Macroscopic cervical and vaginal deciduosis presented as recurrent vaginal bleeding in over 16 of 24 women (57%). Differential diagnoses included miscarriages, cervical pregnancy, placenta previa, and malignancy. Significant antenatal hemorrhages, preterm rupture of membranes, and preterm birth were the most frequent pregnancy complications. Only one of 27 electively performed procedures resulted in biopsy-induced uncontrolled vaginal bleeding (0.04%), suggesting the relative safety of the interventions. Lesion resection led to the cessation of recurrent symptoms in eight of eight patients (100%) compared to eight of 15 women (53%) under observation management. All women with polypoid deciduosis over 1.5 cm entered labor and delivered without complications.

Conclusions. We described the clinical course, pregnancy complications, diagnostic-related challenges, management, and associated outcomes in women with macroscopic cervical and vaginal deciduosis. We supported the analysis with the current state of the problem and discovered gaps for prospective studies.

Categories: Obstetrics/Gynecology

Keywords: antenatal bleeding, polypectomy, decidual polyp, decidual ectopy, systematic review

Introduction And Background

Deciduosis, an extra-uterine transformation of connective tissue into decidual-resembling cells, mainly occurs during pregnancy. Microscopically, 70.2% of biopsies obtained during a cesarean section [1] and 15.2%-34% of cervical cytological smears [2,3], as well as up to 90% of cervical biopsies [4], revealed decidual cells. The incidence of macroscopic lesions is unknown.

Deciduosis is generally considered a benign reaction. However, it might lead to significant pregnancy complications and management challenges. Existing systematic reviews [5-7] listed deciduosis-associated complications, such as spontaneous hemoperitoneum in pregnancy, (peri)appendicitis, bowel perforation, endometriotic lesion decidualization, disruptions of such lesions (especially threatening when approximated to vulnerable areas like uterine vessels and ureters), urinary bladder or ovarian pseudotumor formation, hemothorax, catamenial pneumothorax, etc. However, to our best knowledge, no systematic review has analyzed deciduosis confined to the lower genital tract location and its impact on pregnancy.

Moving externally from the endocervix, deciduosis of the lower genital tract presents as polyp and ectopy, including its papillary, polypoid, and infiltrative forms [8]. Polyp and papillary ectopy arise from the stroma

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under the columnar epithelium and appear as multicolored "beans" and pale grape-like columnar epithelial villi enlargement, respectively. Polypoid ectopy occurs under the columnar and squamous epithelium, frequently includes a transformation zone, and presents as a friable, yellow-brown mass. Infiltrative ectopy originates under the squamous epithelium as multiple small elevations. Lesion ulceration is common.

Studies identified that pregnancy-associated changes in the cervix, including decidual cells or the Arias-Stella reaction, are sometimes mistakenly recognized as atypical [9,10]. Colposcopic impressions can be misleading while performing a biopsy during pregnancy might be risky because of the possibility of excessive bleeding and coincidental pregnancy complications [11]. Contrary to popular belief, it is most important to rule out the coexistence of malignancy in suspicious cases.

Accumulated data suggest that cervical deciduosis increases the risks of late miscarriages and preterm birth because of a premature rupture of membranes [12-14]. Besides, large lesions in labor, especially those that lead to intrapartum bleeding, can raise additional challenges [15-16].

Therefore, this study aims to review the clinical course and management of pregnancies in patients with deciduosis of the lower genital tract. We have included all the possible pregnancy complications and analyzed the incidence of intervention-associated complications, symptoms, and lesion resolution according to the chosen management and, if lesions persisted, the size of the lesions and problems accompanying vaginal delivery. Summarizing these data, we describe the possible challenges, pregnancy complications, and management outcomes. Additionally, we discover knowledge gaps that might serve as a guide for subsequent report descriptions.

Review

Methods

Search Strategy and Selection Process

We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines released in 2020 to prepare a systematic review [17]. Our search strategy, using keywords such as deciduosis, ectopic decidua, ectopic decidual reaction, and ectopic decidualization, was introduced in five databases (PubMed, PubMed Central (PMC), Europe PMC, ScienceDirect, and Google Scholar) and retrieved the references from inception to February 24, 2023. Complete queries and the search results are provided in Table 1.

| Databases | Queries | Results |
|----------------|--|-----------------|
| PubMed | Deciduosis OR "Ectopic decidua" OR "Ectopic decidual reaction" OR "Ectopic decidualization" Filters: Case Reports, Observational Study | 77 ^a |
| PMC | ((Deciduosis) OR "Ectopic decidua") OR "Ectopic decidual reaction") OR "Ectopic decidualization" | 159 |
| Europe PMC | ("Deciduosis" OR "Ectopic decidua" OR "Ectopic decidual reaction" OR "Ectopic decidualization") | 215 |
| ScienceDirect | "Deciduosis" OR "Ectopic decidua" OR "Ectopic decidual reaction" OR "Ectopic decidualization" | 99 ^b |
| Google Scholar | "Deciduosis" OR "Ectopic decidua" OR "Ectopic decidual reaction" OR "Ectopic decidualization" | 980 |

TABLE 1: The databases, search queries, and results

The initial search showed: ^a139 results on PubMed (applied filters: case reports, observational study);^b249 results on ScienceDirect (applied filters: case reports, research articles)

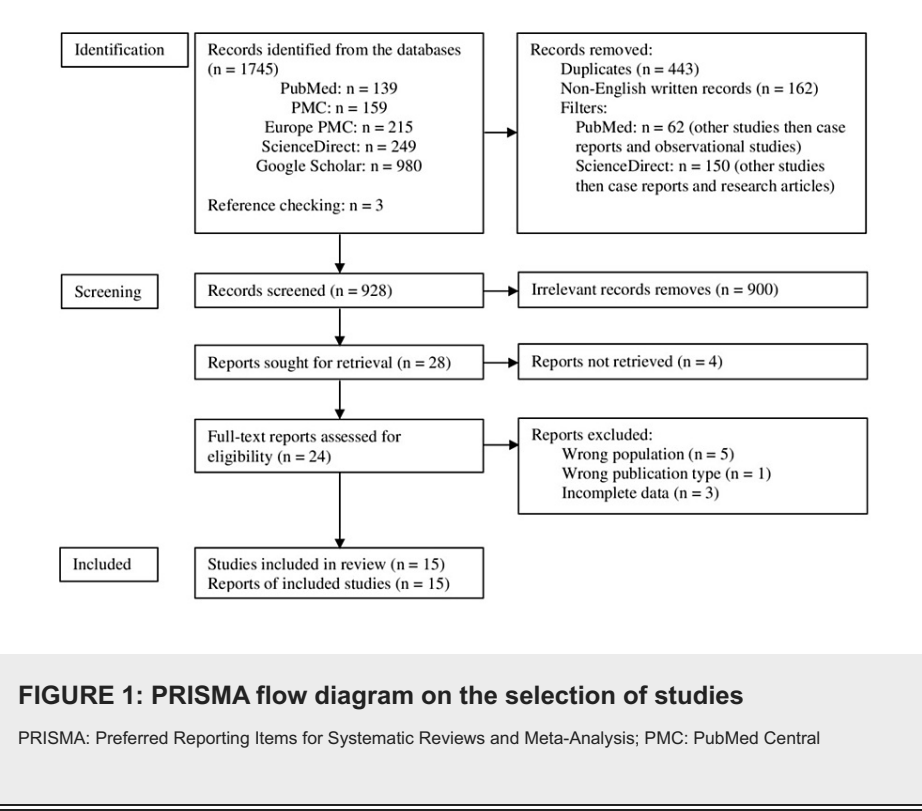
PMC: PubMed Central

Following the search, we uploaded the citations into the EndNote software (Clarivate, Philadelphia, PA, USA) and shared them among the authors (ZB, HD, MS). Then, two reviewers (ZB and HD) independently proceeded with the identification and screening process. They were consulted by a third author (MS) whenever disagreements arose. After removing the duplicates, non-English, and irrelevant records, full-text articles were retrieved and reviewed for eligibility criteria, as provided in Table 2.

| Inclusion criteria | Exclusion criteria |
|---|---|
| 1. Population: Pregnant women with lower genital tract decidualis. | 1. Associated ectopic or molar pregnancy |
| 2. Phenomenon of interest: Clinical course of the pregnancies and unique difficulties | 2. Type of studies: non-primary studies |
| 3. Outcomes: Pregnancy complications and management-related outcomes | 3. 'Grey' literature, including unpublished studies |
| 4. Types of studies: Case reports, case series, and case-control studies | 4. Animal studies |
| 5. Human studies | |
| 6. Time: Published from the inception to February 24, 2023. | |
| 7. Location: Worldwide | |
| 8. Language: Articles written in English | |
| 9. Free full-text articles | |

TABLE 2: Full eligibility criteria

Besides, checking reference lists retrieved three additional studies for the analysis. During the whole process, we did not use any automatic tools. The entire process is shown in Figure 1.



Data Collection and Synthesis

The same reviewers extracted data to a Microsoft Excel (Microsoft Corporation, Redmond, WA, USA) file independently according to the previously chosen variables and outcomes, which were as follows: (1) patients' characteristics included age, parity, preexisting history of cervical pathology and its treatment, and the results of cervical cancer screening; (2) clinical features included location, form, and size of the lower genital tract decidualis, course of previous pregnancies, clinical presentation while establishing the diagnosis, and differential diagnosis; (3) management-related parameters: weeks of gestation (WG), results of the cytology and colposcopy and associated challenges, interventions (biopsy, polypectomy or removal of polypoid masses, or their combinations), and postpartum follow-up results within eight weeks; and (4) outcomes: (a) pregnancy complications, such as significant hemorrhages, pregnancy loss, intraamniotic

infection (IAI) and/or preterm rupture of the membranes (PROM), preterm birth, cesarean section, etc.; and (b) management-associated results (intervention-associated complications, symptom resolution or persistence according to the chosen management, spontaneous regression of lesions during observation, and, if lesions persisted, their size and vaginal birth outcomes).

We made certain assumptions whenever information could not be recovered or clarified. If the authors reported multiple elevations on the cervix, we suspected an *infiltrative form* of decidualosis [18,19]. When the authors described the lesion as a single ectocervical or vaginal "mass," we interpreted it as a *polypoid form* of ectopy [20-22]. We recognized the case of having a decidual polyp during the previous pregnancy as a *polyp* [23]. In one case, it was hard to differentiate a polyp from a potentially papillary form of decidualosis or expelled fragments of the decidua described as the endocervical "grayish membranes" [24]. If *vaginal bleeding* was not followed by any emergent workup, we considered it insignificant. Additional workup to rule out differential nosologies and concerns mentioned in the discussion sections of the articles contributed to the *differential diagnosis* analysis. We also recalculated the patient's *age* based on the provided chronology [25] and the *term of gestation* based on the last menstrual period day or, if unavailable, the confinement date or size of uterus enlargement [22,23]. The "*reassuring*" result of cytology was interpreted as normal [19]. Given the diverse terms of gestation and circumstances of revealing the pathology, we *categorized pregnancies as managed expectantly* if: (1) there were no planned interventions [24,26]; (2) patients underwent urgent or emergent procedures [27,28]; (3) unprovoked pregnancy complications led to pregnancy termination [20,25]; or (4) patients presented initially after 37WG [15,16,21,23]. When reports included a scheduled remote postpartum follow-up for cervix re-evaluation within eight weeks, we suspected *lesion persistence* [19,22,28]. We excluded underreported and unrestored information from the corresponding analysis, marking them as "not reported" or "not applicable." The extracted data is organized in Tables 3-5.

| Author, Year (Country) | Age | Parity | Preexisting cervical pathology/treatment and cancer screening | Location | Form (size) | Symptoms at the time of revealing the pathology | Preexisted pregnancy course | Differential diagnosis |
|---------------------------------------|-----|--------|---|---------------------------|------------------------------|---|-----------------------------|-----------------------------------|
| Oh et al., 2022 (Korea) [20] | 33 | 0 | NR | Upper third of the vagina | Polypoid (RV DIE 6.1x4.1 cm) | Recurrent VB | Recurrent VB | Vaginal cancer, DIE malignization |
| Batkoska et al., 2022 (Slovenia) [25] | 27 | 0 | CIN3/LLETZ 5Y prior | Cervix | Polyp (2.2x1 cm) | VB | NR | None |
| | 28 | 0 | CIN3/LLETZ 6Y prior | Cervix | Polyp (4x1 cm) | Malodorous VD | NR | None |
| | 29 | 0 | CIN3/LLETZ 7Y prior | Cervix | Polyp (4x2 cm) | Resolved VB | NR | None |
| Verma et al., 2022 (India) [18] | 28 | 2 | NR | Cervix | Infiltrative (0.5-to-1.5 cm) | Resolved VB | NR | Cervical cancer |
| Buttery et al., 2021 (Australia) [16] | 22 | 0 | NR | Cervix | Polypoid (large) | NR | NR | Placenta previa |
| Mangla et al., 2021 (India) [27] | 28 | 0 | NR | Cervix | Polyp (2x2 cm) | Recurrent VB | Recurrent VB | None |
| Xiaoyin et al., 2018 (China) [26] | 32 | 1 | NR | Cervix | Polyp (0.8 cm) | VB | NR | NR |
| | 25 | 0 | NR | Cervix | Infiltrative/Polypoid (1 cm) | VB | NR | NR |
| | 27 | 0 | NR | Cervix | Ulcerated + Polyp | VB | NR | NR |
| | 37 | 1 | NR | Cervix | Polyp (2 cm) | Recurrent VD/VB | Recurrent VD/VB | NR |
| | 28 | 0 | NR | Cervix | Infiltrative/Polypoid (2 cm) | VB | NR | NR |
| | 22 | 0 | NR | Cervix | Papillary + Polyp | Recurrent VD/VB | Recurrent VD/VB | NR |
| | 37 | 0 | NR | Cervix | Polypoid (1.5 cm) | VD/VB | NR | NR |
| | 29 | 0 | NR | Cervix | Infiltrative + Polyp (2 cm) | Recurrent VB | Recurrent VB | NR |
| | 27 | 0 | NR | Cervix | Ulcerated/Polypoid (1.5 cm) | Recurrent VB | Recurrent VB | NR |
| | 26 | 0 | NR | Cervix | Polyp (1 cm) | VB | NR | NR |

| | | | | | | | | |
|--|----|---|---|------------------------------------|---|---------------------|----------------|--|
| | 23 | 0 | NR | Cervix | Papillary/Polypoid (2 cm) | Recurrent VB | Recurrent VB | NR |
| van Diepen et al., 2015 (Netherlands) [19] | 34 | 0 | CIN3/LLETZ 1Y prior; Cytology: Normal 0.5Y and 1Y prior | Cervix | Infiltrative (0.5-to-1.5 cm) | VB | NR | Polyps, cervical adenoma |
| Oladipo et al., 2005 (UK) [28] | 28 | 0 | Insignificant history; Cytology: Normal 1Y prior | Cervix | Polypoid (4×4 cm) | VB of “300 ml” | “Uneventful” | Placenta previa or abruption |
| Gornall et al., 2000 (UK) [15] | 23 | 0 | Cytology: Normal 2Y prior | Cervix | Polypoid (8 cm) | PROM | “Offensive” VD | Cervical cancer |
| Armenia et al., 1964 (USA) [23] | 22 | 2 | Unremarkable cervix at 24WG | Cervix | Polypoid | None | Unremarkable | Primary reticulum cell sarcoma |
| | 22 | 3 | Previous pregnancy: 1-cm decidual polyp | Cervix | Polyp (6 cm) | VB | VB | “Undifferentiated tumor of reticuloendothelial origin” |
| Orr et al., 1961 (Northern Ireland) [29] | 26 | 1 | “Erosion”/Diathermy | Cervix + Upper third of the vagina | Polypoid (large) | Recurrent VB | Recurrent VB | Placenta previa, carcinoma |
| Mathie, 1957 (UK) [30] | 39 | 2 | NR | Upper third of the vagina | Polypoid (large) | None | “Uneventful” | Cervical, then vaginal carcinoma |
| Spivack, 1949 (USA) [24] | 31 | 1 | NR | Cervix | Infiltrative + “grayish membranes” (1.5 cm) | Worsened leukorrhea | Leukorrhea | Miscarriage, ectopic pregnancy |
| Lapan, 1949 (USA) [22] | 33 | 0 | “Normal” | Cervix + Upper third of the vagina | Polypoid (large) | Profuse VB | VB worsening | Cervical cancer |
| | 35 | 1 | NR | Upper third of the vagina | Polypoid (large) | None | NR | Vaginal cancer |
| | 31 | 1 | “Normal” | Cervix | Polypoid (large) | None | NR | Anaplastic cancer |
| Klein et al., 1946 (USA) [21] | 23 | 0 | 12WG: No polyps, “erosions”, or growths | Cervix | Polypoid (2 cm) | VB (“cupful”) | “Uneventful” | Placenta previa, cervical cancer |

TABLE 3: Data extraction of the clinical characteristics

NR: not reported; RV: rectovaginal; DIE: deep infiltrative endometriosis; VB: vaginal bleeding; CIN3: cervical intraepithelial neoplasia (grade 3); LLETZ: large loop excision of the transformation zone; Y: year(s); VD: vaginal discharge; PROM: preterm rupture of membranes; WG: weeks of gestation

| Author, Year (Country) | WG ^a | Cytology | Colposcopy | Biopsy(ies) | Ectomy of lesions | Postpartum follow-up within 8 weeks |
|---------------------------------------|-----------------|----------|------------|-----------------------|--------------------|-------------------------------------|
| Oh et al., 2022 (Korea) [20] | 34WG | NR | NR | N/A (Active VB) | None | NR |
| Batkoska et al., 2022 (Slovenia) [25] | 6WG | NR | Polyp | None | Polypectomy | N/A (Removed) |
| | 10WG | NR | NR | None | None | N/A (Removed vs. Regressed) |
| | 7WG | NR | NR | None | Polypectomy | N/A (Removed) |
| Verma et al., 2022 (India) [18] | 32WG | NR | NR | Biopsy | None | Speculum: Normal; Cytology: NILM |
| Buttery et al., 2021 (Australia) [16] | 41WG | NR | NR | None (Intraoperative) | None | NR |
| Mangla et al., 2021 (India) [27] | 20WG | NR | NR | None | Urgent polypectomy | N/A (Removed) |

| | | | | | at 24WG | |
|--|-------|--------|--|--|-------------------------------------|--|
| Xiaoyin et al., 2018 (China) [26] | 8WG | NILM | Polyp | None | None | N/A (Regressed) |
| | 21WG | NILM | Ectopy | Biopsy | Polypectomy ^b at 24WG | N/A (Removed) |
| | 19WG | NILM | Polyp/Ectopy | Biopsy | None | N/A (Regressed) |
| | 10WG | NILM | Polyp | Biopsy | Polypectomy at 12WG | N/A (Removed) |
| | 15WG | NILM | Ectopy | Biopsy | None | NR |
| | 16WG | NILM | Polyp/Ectopy | Biopsy | Polypectomy ^b at 19WG | N/A (Removed) |
| | 7WG | NILM | Ectopy | Biopsy | Polypectomy ^b at 12WG | N/A (Removed) |
| | 23WG | NILM | Polyp/Ectopy | Biopsy | Polypectomy ^b at 27WG | N/A (Removed) |
| | 32WG | NILM | Ectopy | Biopsy | None | NR |
| | 8WG | NILM | Polyp | None | None | N/A (Regressed) |
| | 28WG | NILM | Ectopy | Biopsy | Polypectomy ^b at 31WG | N/A (Removed) |
| van Diepen et al., 2015 (Netherlands) [19] | 11WG | Normal | Acetic acid: "no abnormalities" | Colposcopy-guided biopsy at 25WG | None | Speculum: Almost resolved; Cytology: Normal |
| Oladipo et al., 2005 (UK) [28] | 28WG | NR | Unsatisfactory Acetic acid: "grayish-white", fine punctuations, "atypical vessels" | Colposcopy-guided, multiple biopsies (Urgent settings) | None | Colposcopy: Normal |
| Gornall et al., 2000 (UK) [15] | 38WG | NR | NR | Biopsies | None | Speculum: Normal; Colposcopy: Normal |
| Armenia et al., 1964 (USA) [23] | 39WG | NR | N/A (Old study) | NR | None | Hysterectomy: 0.1×0.8 cm nodule |
| | 15WG | NR | N/A (Old study) | Biopsy; Biopsies at 17WG | None | Cold knife conization: normal |
| Orr et al., 1961 (Northern Ireland) [29] | 36WG | NR | N/A (Old study) | Biopsy | None | Speculum: Almost resolved |
| Mathie, 1957 (UK) [30] | 28WG | NR | N/A (Old study) | Biopsy | None | Speculum: Normal |
| Spivack, 1949 (USA) [24] | 10WG | NR | N/A (Old study) | None (pseudobiopsy ^c) | None | Speculum: "Inflamed and eroded" |
| Lapan, 1949 (USA) [22] | 12WG | NR | N/A (Old study) | Biopsy | None | Speculum: "Erosion"; Biopsy: Diffuse adenomatosis |
| | 12WG | NR | N/A (Old study) | Biopsy | None | Speculum: Normal |
| | <12WG | NR | N/A (Old study) | Biopsy | None | Speculum: Normal |
| Klein et al., 1946 (USA) [21] | 41WG | NR | N/A (Old study) | None | None | Speculum: "Erosion"; Biopsy: Normal |

TABLE 4: Data extraction of the management results

WG: weeks of gestation; NR: not reported; N/A: not applicable; VB: vaginal bleeding; NILM: negative for intraepithelial lesion or malignancy; cm: centimeter(s)

^aThe column "WG" refers to the initial revealing of pathology. The term of gestation for delayed or additional procedures was mentioned additionally in the corresponding fields.

^bThe term polypectomy included polypectomy and/or removal of the ectopic mass.

^cThe term pseudobiopsy means gentle tissue removal without obtaining a baseline layer.

| Author, Year (Country) | Pregnancy complications | Pregnancy course and immediate postpartum period | | | Vaginal birth: delivered/complication (peripartum size of the lesions) |
|---|---|---|---|--|--|
| | | Planned procedure: Uneventful/Complication | Observation (including biopsy)/Polypectomy: Symptom(s) resolution or recurrence | Regression of lesions (if no ectomy was performed) | |
| Oh et al., 2022 (Korea) [20] | VB/Shock, Uterine scar, Preterm birth | N/A (Emergent settings) | Observation: Recurrent VB | N/A (Emergent C-section) | N/A (Emergent C-section) |
| Batkoska et al., 2022 (Slovenia) [25] | N/A (Remote missed abortion) | Polypectomy: Uneventful | Polypectomy: VB resolved | N/A (Removed) | N/A (Missed abortion) |
| | IAI/PROM, Late pregnancy loss | N/A (None) | Observation: Recurrent VB and UTI | N/A (Unknown: Removed vs. Regressed) | N/A (Late pregnancy loss) |
| | N/A (Polypectomy) | Polypectomy: Uneventful | Polypectomy: VB resolved | N/A (Removed) | N/A (Removed) |
| Verma et al., 2022 (India) [18] | Uterine scar, Preterm birth | Biopsy: Uncontrolled VB | Observation: NR | N/A (Urgent C-section) | N/A (Urgent C-section) |
| Buttery et al., 2021 (Australia) [16] | Uterine scar | N/A (Intraoperative) | Observation: NR | Persisted | Early stage of labor complicated by VB/fetal distress (entire posterior lip of the cervix) |
| Mangla et al., 2021 (India) [27] | VB/Shock | N/A (Urgent polypectomy) | Observation: Recurrent VB; Urgent polypectomy: NR | N/A (Removed) | N/A (Removed) |
| Xiaoyin et al., 2018 (China) [26] | NR | N/A (None) | Observation: NR | Regressed at 12WG | N/A (Regressed) |
| | NR | Biopsy: Uneventful; Polypectomy ^a : Uneventful | Polypectomy ^a : Recurrent VB resolution | N/A (Removed) | N/A (Removed) |
| | NR | Biopsy: Uneventful | Observation: Recurrent VB | Regressed at 35WG | N/A (Regressed) |
| | NR | Biopsy: Uneventful; Polypectomy: Uneventful | Polypectomy: Recurrent VB resolution | N/A (Removed) | N/A (Removed) |
| | NR | Biopsy: Uneventful | Observation: Recurrent VB | Persisted | NR |
| | NR | Biopsy: Uneventful; Polypectomy ^a : Uneventful | Polypectomy ^a : Recurrent VB resolution | N/A (Removed) | N/A (Removed) |
| | NR | Biopsy: Uneventful; Polypectomy ^a : Uneventful | Polypectomy ^a : Recurrent VB resolution | N/A (Removed) | N/A (Removed) |
| | NR | Biopsy: Uneventful; Polypectomy ^a : Uneventful | Polypectomy ^a : Recurrent VB resolution | N/A (Removed) | N/A (Removed) |
| | NR | Biopsy: Uneventful; Polypectomy ^a : Uneventful | Polypectomy ^a : Recurrent VB resolution | N/A (Removed) | N/A (Removed) |

| | | | | | |
|---|--|---|---|-------------------|---------------------------------|
| | NR | Biopsy: Uneventful | Observation: Recurrent VB | Persisted | NR |
| | NR | N/A (None) | Observation: NR | Regressed at 20WG | N/A (Regressed) |
| | NR | Biopsy: Uneventful; Polypectomy ^a : Uneventful | Polypectomy ^a : Recurrent VB resolution | N/A (Removed) | N/A (Removed) |
| van Diepen et al., 2015 (Netherlands) [19] | N/A (C-section due to failure to progress) | Biopsy: Uneventful | Observation: NR | Persisted | N/A (Failure to progress) |
| Oladipo et al., 2005 (UK) [28] | Severe VB | N/A (Urgent settings) | Observation: "Without further complications" | Persisted | Delivered |
| Gornall et al., 2000 (UK) [15] | IAI/PROM, Uterine scar | Biopsies: Uneventful | Observation: "Offensive" VD | Persisted | N/A (Emergent C-section) |
| | None | NR | Observation: "Uneventful" | Persisted | Delivered (1.5×0.6×0.4 cm) |
| Armenia et al., 1964 (USA) [23] | None | 15WG Biopsy: Uneventful; 17WG Biopsies: Uneventful | Observation: NR | Persisted | Delivered (2 cm) |
| Orr et al., 1961 (Northern Ireland) [29] | N/A (None) | Biopsies: Uneventful | Observation: Recurrent VB | Persisted | Delivered (large) |
| Mathie, 1957 (UK) [30] | "Mild toxemia" | Biopsies: Uneventful | Observation: Provoked VB | Persisted | IOL followed by mild VB (large) |
| Spivack, 1949 (USA) [24] | N/A (None) | N/A (Pseudobiopsy ^b) | Observation: Recurrent VB/Persisted leucorrhea | NR | NR vs. Regressed? |
| | N/A (None) | Biopsies: Uneventful | Observation: Provoked profuse VB | Persisted | Delivered |
| Lapan, 1949 (USA) [22] | N/A (None) | Biopsies: Uneventful | Observation: "Uneventful" | NR | NR vs. Regressed? |
| | N/A (None) | Biopsies: Uneventful | Observation: NR | Persisted | Delivered |
| Klein et al., 1946 (USA) [21] | Profuse VB | Early postpartum biopsy: VB | Observation: "Uneventful" | Persisted | Delivered (2 cm) |

TABLE 5: Data extraction of the outcomes

VB: vaginal bleeding; N/A: not applicable; C-section: caesarean section; IAI: intraamniotic infection; PROM: preterm rupture of membranes; UTI: urinary tract infection(s); NR: not reported; WG: weeks of gestation; VD: vaginal discharge; cm: centimeter(s); IOL: induction of labor

^aThe term polypectomy included polypectomy and/or removal of the ectopic mass.

^bThe term pseudobiopsy means gentle tissue removal without obtaining a baseline layer.

After completing the data extraction, two reviewers (ZB and HD) critically appraised the studies independently by using the CAsE REport (CARE) assessment tool for case reports [31] and the Joanna Briggs Institute (JBI) critical appraisal tools for case series [32]. The third reviewer (MS) resolved doubts and disagreements. The studies that scored 70% or higher contributed to our systematic review. This threshold was lowered to 60% for the studies published before 2013, as we did not want to lose clinically relevant information due to differences in the requirements of reporting cases.

We summarized clinically relevant qualitative variables by frequencies and presented them as percentages supported by a numerator and denominator. Continuous variables were presented as the mean and range in a normal data distribution and the median and interquartile range in a non-normal data distribution.

We did not develop the protocol and register the systematic review at the International Prospective Register of Systematic Reviews (PROSPERO) due to the short timeline for its completion. The protocol was substituted with data extraction tables in Microsoft Excel and subsequent analysis.

Results

Our search strategy identified 1745 records. After removing the duplicates ($n = 443$), foreign language articles ($n = 162$), and, partially, irrelevant reports whenever filters could be applied ($n = 212$), 928 records underwent screening. The inability to retrieve four reports limited our assessment for eligibility to only 24 records; of those, we excluded nine studies due to the wrong population ($n = 5$) [33-37], wrong publication type ($n = 1$) [8], and incompleteness of the presented data for the analysis ($n = 3$) [14,38,39]. Finally, 15 of 17 studies scored from 63% to 100% during the critical appraisal process and were subject to analysis [15,16,18-30]; 14 case reports, and one case series describing 30 cases.

Patients' Characteristics

The mean patient age was 28 years (± 4.86). Nulliparous women represented the majority - 18 of 30 women (60%). Among preexisting pathologies, there was a history of cervical intraepithelial neoplasia (grade 3) treated with loop electrosurgical excision of the transformation (four cases), cervical "erosion" treated with diathermy (one case), and recurrent decidual polyps (three cases).

Clinical Presentation

Lesions were localized at the cervix (83%, 25 of 30 reports), the upper third of the vagina (10%, three of 30 reports), or both locations (7%, two of 30 cases). Among the 22 reported cases of ectopies (73%), 40% accounted for polypoid (12 cases), 10% were infiltrative (three cases), and 23% were coexisting forms (seven cases).

Clinically, decidualosis presented an accidental finding only in four of 29 patients (14%). The rest of the patients complained of leukorrhea or infectious vaginal discharge (21%, six of 29 women) and/or vaginal bleeding, which was the chief complaint in 22 of 29 women (76%) and had a recurrent character in more than 16 of 24 patients (57%) based on the previous and subsequent course of the pregnancies.

Differential diagnoses included threatened abortion and ectopic pregnancy (one case), cervical adenoma (one patient), placenta previa (four cases), and cervical or vaginal malignancy (11 cases), including one patient with suspicious rectovaginal deep infiltrative endometriosis malignization.

Management

Decidualosis was revealed before 24WG in 18 of 30 pregnancies (60%). All reported cytological findings were normal. Only one study documented the details of colposcopy. According to that study, the possible challenges are incomplete visualization of the transformation zone, "grayish-white" epithelium after applying acetic acid, and "atypical vessels."

Eleven of the patients were managed expectantly (37%). The rest of the pregnant women underwent a total of 27 planned procedures: before 24WG (12 cases), during 24-to-33 6/7WG (seven cases), and after 34WG (eight cases). In the eight weeks postpartum, five of 12 patients (42%) had residual findings, including "erosions" and diffuse adenomatosis.

Outcomes

Studies reported the following complications of the pregnancies: significant antenatal bleeding (four studies), late abortion (one case), IAI and/or PROM (two cases), preterm birth (two cases), and operative delivery with uterine scar formation (four patients).

Among the 27 scheduled procedures, only one case of uncontrolled vaginal bleeding occurred at 32WG (0.04%).

Observation, including pregnancies managed expectantly or biopsied, was followed by recurrent symptoms (vaginal bleeding, urinary tract infections, vaginal discharge) or uneventfully (none, single, or provoked episode) in eight (53%) and seven (47%) women, respectively. Recurrent vaginal bleeding resolved in all eight cases (100%) of performed polyp or polypoid mass ectomies.

Spontaneous regression of lesions during observation happened in 20% (three of 16 patients) at 12WG, 20WG, and 35WG. All of these lesions were polyps, including one case of ulcerated ectopy.

Nine studies reported lesion persistence until vaginal birth. Almost all of these women had large polypoid lesions during their pregnancies. Among them, six women entered labor with the reported size of the lesions ranging from 1.5-2 cm to "large." None of the cases were complicated with significant intrapartum hemorrhage, although one study reported fetal distress of unknown etiology in the early stage of labor.

Discussion

Deciduosis of the lower genital tract was observed in women of 22 to 39 years of age, appearing on the cervix (83%) and/or vaginal fornices. Unfortunately, most case reports did not report the prior history of cervical or vaginal pathologies, limiting the opportunity to suggest the recurrence nature of the pathology, although decidual polyps demonstrated the tendency [23,25].

We noted that macroscopic cervix and/or vaginal fornix deciduosis was most commonly symptomatic, presenting as recurrent painless vaginal bleeding in more than half of the patients. Three pregnancies with lesions exceeding 2 cm in diameter were complicated by spontaneous antenatal hemorrhage of over 250 ml between 24WG and 34WG [20,27-28]. According to the literature, the lesions start regression around 25WG and, in 60%-70%, disappear completely by 38WG [8]. Because of this, it seems reasonable to diagnose the condition early, while ruling out cancer and locating the placenta, and consider respiratory distress syndrome prevention, especially if a biopsy is unavoidable during the late term of gestation.

Reviewing a previous history of cervical dysplasia, its treatment, and subsequent surveillance, including cervical cytology obtained in the first trimester of pregnancy, might help establish the diagnosis while minimizing the risks associated with cervical biopsy. For example, in one study [19], a patient underwent treatment for cervical intraepithelial neoplasia (grade 3) with subsequent normal cytological results before conception. She developed an infiltrative form of deciduosis, followed by reassuring cytological plus colposcopy surveillance until 25WG when the biopsy was performed because of the growth of the lesions. This case highlights the importance of cervical cancer screening before 20WG [40] when the lesions do not obscure the transformation zone and awareness of the pathology (in this case, the infiltrative form does not include the transformation zone and is multifocal form, therefore can allow avoiding a biopsy). Moreover, the absence of a high-grade pattern, surrounding foci of lower-grade abnormalities, and intensive necrosis of the lesions during colposcopy might help to avoid biopsy if local guidelines do not require it, regardless of the dense whitening of the lesions. However, it is the polypoid form that seems to be the most problematic one from a differential perspective and the most reported form of ectopy (58%), as it includes a transformation zone. In addition to taking a history and performing the mentioned diagnostics, this form of deciduosis presents as confusingly friable compared to relatively solid cancer. The less frequently reported form of ectopy was the papillary one, which may be the less recognizable form of deciduosis, as likely shown in an example [24]. Still, in this case, expelled fragments of the decidua are a suitable explanation too.

Previous studies noted that performing a biopsy of the cervix during pregnancy is generally safe in terms of the occurrence of significant bleeding or pregnancy complications [40-42]. We obtained similar findings based on 27 electively performed procedures before 24WG (44%), during 24-to-33 6/7WG (26%), and after 34WG (30%). Our analysis also reflects the relative safety of biopsy decidual lesions that might be more prone to hemorrhages due to their friability, frequent association with chronic inflammation, and susceptibility to necrosis [24], especially with pregnancy progression [8]. For instance, the included studies reported severe antepartum hemorrhage [20,27,28], profuse bleeding provoked by gynecologic evaluation [21], and biopsy-induced uncontrolled bleeding [18] in women between 24-41 WG. These lead to two conclusions: (1) a cervical biopsy or stiff brush procedure is needed if there are any doubts regarding cervical cancer [11], and (2) respiratory distress prophylaxis may be considered if the procedure is planned after 24WG. Lately, remote studies have indicated that misleading results might lead to unnecessary procedures such as cervical conization during pregnancy [39], postpartum hysterectomy, and cold knife conization [23].

The authors cite that cervical and/or vaginal deciduosis does not require special pregnancy management unless complications develop. However, there are a few considerations. First, a retrospective cohort study of 550 pregnant women with cervical polyps noted that 45.45% of cases accounted for decidualized ones, which led to a greater frequency of pregnancy complications than non-decidualized polyps (28.1% vs. 6.1%) [43]. Thus, managing decidualized polyps in certain circumstances can be distinct from those without changes. Second, decidual polyp or polypoid mass ectomies might be helpful in resolving recurrent symptoms, though it is uncertain who might benefit from the procedure and whether resection reduces the risk of pregnancy complications. Perhaps pregnant women over 11WG with a polyp width greater than 11 mm, recurrent vaginal bleeding (in our opinion, recurrent inflammatory discharges in the setting of either multicolored or fragile lesions), and visualized roots could be good candidates [25,44-46]. At the same time, one study noted that spontaneous regression of the lesions, which is common, did not reduce the risk of cervical insufficiency and pregnancy loss [13]. Again, the authors did not evaluate these outcomes based on the histological type of the polyps. Lastly, one case report showed a 6-to-2 cm polyp size reduction in two months on local treatment with Neosporin [23]. Although a natural regression process can explain it, similar options could be considered when the risk of symptomatic lesion removal is high (e.g., non-visualized roots) and infected and edematous lesions are suspected.

In labor, macroscopic polypoid lesions, especially large ones (e.g., covering the entire posterior lip or an 8-cm mass), are inflamed, and those that are initially revealed in the peripartum period concern providers regarding intrapartum bleeding and its differential diagnosis [15,16]. However, at least six old studies with the size of lesions between 1.5 and large cm were not complicated by significant intrapartum hemorrhage. In one report, the 2-cm polypoid lesion remained "silent" even in the early postpartum period until biopsy [21]. Finally, accelerated regression of cervical deciduosis is to be expected shortly after delivery and complete

lesion resolution by six weeks after delivery. According to our analysis, some residual findings are possible.

Limitations

Our systematic review has a few limitations. There is a risk of publication bias associated with reporting only recognized and successfully managed cases. Of note, older studies reported mismanagement issues more openly. Although improved antenatal management and advanced diagnostic opportunities might explain it, the rarity of macroscopic lesions, the lesions' ability to appear at a later term of gestation, and uncertainty in managing some situations perplex providers [16,18]. We analyzed only studies published in English, which could lead to losing important information. Besides, some studies mainly described cases around the episode of active management, missing the information essential for a thorough evaluation and, consequently, limiting current knowledge on the diagnostic pitfalls that can be addressed in prospective case reports. We also recovered or clarified some missed and descriptive data (discussed in the Materials and Methods section) that unlikely impacted our results significantly. Of course, considering the rarity of the condition, we could include only studies with a lower grade of evidence. However, we covered an important segment useful for providers and prospective studies.

Conclusions

We described the clinical course, all pregnancy complications, and management-associated outcomes in pregnant women with macroscopic cervical and/or vaginal decidualis. Most frequently, it presented as recurrent vaginal bleeding episodes that can be substantial after 24WG, requiring the exclusion of placenta previa, cervical pregnancy, and malignancy, as well as consideration of respiratory distress syndrome prophylaxis (for instance, in cases of large lesions, planned procedures, and successfully treated hemorrhagic episodes). Pregnancy complications included significant antenatal hemorrhages, PROM, uncontrolled bleeding-associated late abortion or preterm birth, and operative delivery. Performing cervical cancer screening before 20WG, recognizing different forms of decidualis, and confusing the friability of the lesions can minimize the risks related to performing a biopsy, which seems avoidable in most situations. However, a biopsy is necessary if there is any doubt regarding cancer (or guideline requirements), and it seems safe to biopsy decidualized lesions, especially before 24WG. Conservative management of the cases is commonly accepted, while the benefits and indications of the excision of the lesion require further evaluation. There are no reports of associated significant intrapartum hemorrhages in women with polypoid ectopies over 1.5 cm, which is a safe delivery route, although it might be individualized in some settings.

This review can serve as a standardized guideline for reporting all pertinent information in future case reports, filling the knowledge gap on diagnostic and management challenges in the context of current technological advancements and prenatal care standards. It can also be a quick source of information in the search for similar cases. There is a need to report cases of management concerning decidualized lesions in labor, regardless of their successful and complicated resolution. An interesting direction is investigating the debatable problem of managing cervical polyps in the presence or absence of decidualized changes.

Additional Information

Disclosures

Conflicts of interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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