Subclinical endometritis after first-trimester abortion

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Abstract

Background: Endometritis is a severe complication occurring after the termination of pregnancy. It occurred at variable rates after first-trimester abortion. Variable diagnostic methods with variable accuracies are reported.

Aim: to detect endometritis after medical and surgical termination of first-trimester abortion using different diagnostic methods.

Methods: This cross-sectional study was conducted at the obstetrics and gynecology department at Fayoum university from May 2018 to February 2020. The study recruited 100 women divided into two groups. Groups A and B included fifty patients who had medical and surgical evacuation of first-trimester abortion, a history of unexplained delayed conception for at least one year, and recurrent miscarriage. Recruited women were subjected to history taking, laboratory investigation, pelvic examination, trans-vaginal ultrasonography, and endometrial sampling. An office hysteroscopy was arranged during the follicular phase of the menstrual cycle. This was followed by two endometrial samples using the Pipelle (Pipelle de Cornier, CCD).

Results: There was an insignificant difference between group A and group B regarding H&E examination by Hysteroscopy and Pipelle and immunostaining examination by Pipelle (P-value > 0.05);. At the same time, it points to a statistically significant difference between group A and group B regarding Immunostaining examination by Hysteroscopy (P-value =0.029). Endometritis was more significantly evident in Immunostaining examination by hysteroscopy in group B than in group A (40% vs. 20%, respectively). The diagnostic accuracy of Immunostaining examination by hysteroscopy was significant (P-value = 0.028).

Conclusion: Endometritis occurs significantly after surgical termination of first-trimester abortion. Hysteroscopic guided biopsy followed by immunohistochemistry was associated with high diagnostic accuracy for endometritis.

Key words: endometritis; abortion; immunostaining; hysteroscopy.

Introduction

Endometritis is defined as inflammation of the endometrium, which lines the uterine cavity. It is considered a pelvic inflammatory disease (1). It occurs due to ascending infection from the genital tract; however, after pregnancy, it occurs due to retained products of conception (RPC) (2). After an abortion, the risk increases due to cervical opening, fetal tissue and blood clots, and uterine instrumentation (3).

First-trimester abortion could be managed surgically or medically. Surgical termination would be associated with infection, uterine perforation, and Asherman syndrome, while; medical termination was associated with avoiding surgical intervention, failed evacuation, and increased bleeding (4). The development of intrauterine synechia was related to endometritis (5). Other reported changes included polyp formation and vascular changes created by endometritis, and as a result, endometrial receptivity was impaired (6). The diagnosis was confirmed by plasma cell infiltration in endometrial biopsies (7). The diagnosis was further confirmed by immunohistochemical staining of endometrial samples (8). Given that endometritis would lead to infertility (9), the current study evaluated endometritis after two first-trimester pregnancy termination methods.

Methods

This cross-sectional study was conducted at the obstetrics and gynecology department at Fayoum university from May 2018 to February 2020. The study recruited 100 women divided into two groups. Group A included fifty patients who had medical evacuation by misoprostol due to a first-trimester abortion, a history of unexplained delayed conception for at least one year, and/or recurrent miscarriage following the medical evacuation. Group B involved fifty patients who had surgical evacuation due to first-trimester abortion and had a history of unexplained delayed conception and/or recurrent miscarriage.

Women aged ≥40 years, with infertility related to a known cause, with recurrent miscarriage due to a known cause, with oxytocin-induced first-trimester abortion, with a history of second-trimester abortion, and those refusing to participate in the study were excluded.

Recruited women were subjected to: -

- History taking included name, age, residence (urban or rural), gravidity, parity, the number of miscarriages, history of evacuation of the products of conception, and method of evacuation, whether medically by misoprostol or surgically by dilatation and evacuation.
- Laboratory investigation: qualitative beta-human chorionic gonadotrophin (B-HCG) to exclude ongoing pregnancy.
- Pelvic examination to detect the position and size of the uterus, vaginal abnormalities, pelvic infection, and cervical polyps.
- Transvaginal ultrasonography (TVS) to exclude organic causes of abortion and delayed conception.
- Endometrial sampling: First, an office hysteroscopy was arranged during the follicular phase of the menstrual cycle (days 6–12), getting a panoramic view of the uterine cavity, the endometrium, and tubal ostia. This was followed by two endometrial samples using the Pipelle (Pipelle de Cornier, CCD). The samples were collected in two separate tubes filled with formalin and normal saline NaCl 0.9% with a ratio of 1:10, respectively.

All specimens were submitted to the same laboratory and analyzed by the same pathologist, utterly ignorant of the hysteroscopic results.

Formalin-fixed biopsies were embedded in paraffin-forming blocks. Each block was sliced into two four-micron sections, one of which was stained with Haematoxylin and Eosin for standard histological inspection. The other was immunostained for Syndecan-1 (CD138) to show plasmacytes.

Pathological diagnostic criteria for chronic endometritis

- For HE-stained specimens: At least five typical plasma cells were visible in the endometrial stroma for the diagnosis of chronic endometritis (10).
- For Immunohistochemically stained specimens: in each 400 x magnification field, five or more typical plasma cells were observed in the endometrial stroma for the diagnosis of chronic endometritis (11).

Statistical analysis

Data were coded and entered using SPSS (Statistical Package for the Social Sciences) version 25. Data were summarized using median, minimum and maximum in quantitative data and using frequency (count) and relative frequency (percentage) for categorical data. Comparisons between quantitative variables were made using the non-parametric Mann-Whitney test. For comparing categorical data, Chi-square ($\chi 2$) test was performed. The exact test was used when the expected frequency was less than 5. P value was considered significant when < 0.05. ROC curve was constructed with the area under curve analysis performed to detect the best cutoff value.

Results

One hundred and nine women were eligible for the study. Nine patients refused to participate in the study, leaving 100 women for the final analysis. Patients were allocated into two groups according to their history of evacuation of first-trimester abortion, with 50 patients in each group.

There was no statistically significant difference between both groups regarding age, gravidity, parity, and residence. (P-value > 0.05) (Table I).

Table (II) showed an insignificant difference between group A and group B regarding H&E examination by Hysteroscopy and Pipelle and immunostain examination by Pipelle (P-value > 0.05);. At the same time, it points to a statistically significant difference between group A and group B regarding Immunostain examination by Hysteroscopy (P-value =0.029). Endometritis was more significantly evident in Immunostaining examination by hysteroscopy in group B than in group A (40% vs. 20%, respectively).

There was an insignificant difference between Hysteroscopy and Pipelle regarding H&E examination and Immunostaining examination in both groups (P-value > 0.05 each)

The diagnostic accuracy of Immunostaining examination by hysteroscopy was significant (P-value = 0.028). Sensitivity, specificity, -ve prediction, +ve prediction, accuracy, and the likelihood ratio of Immunostaining examination by hysteroscopy are 40, 80, 66.7, 57.1, 63.14%, and 4.83, respectively (Table III).

Discussion

Endometritis occurred in a higher proportion after surgical evacuation of pregnancy rather than a medical evacuation. The difference was insignificant, but when hysteroscopy and Syndecan-1 were utilized in combination, 40% of cases were detected. This agreed with previous study results using the same diagnosis technique (12). An earlier study reported lower infection rates after medical termination of first-trimester abortion (13), which further decreased after adopting the oral route of misoprostol administration (14). This would be rendered to the vaginal

flora gaining access to the uterine cavity. Additionally, uterine instrumentation increased this risk (15).

The current study adopted the threshold of at least five plasma cells for the diagnosis of endometritis according to previously published studies (16, 17). Different endometritis rates were reported previously, which was rendered to the different diagnostic methods, which only depended on histological detection of plasma cells (18).

Endometritis was better demonstrated with combined hysteroscopy and immunohistochemistry. It also demonstrated better diagnostic accuracy than other tools, which was different from other studies (9, 19) due to different sample sizes, surgical experience, and ethnicity. This was attributed to the increased false negative rates by the Pipelle biopsy as it is a blind technique for obtaining tissue that might miss small polyps. Additionally, these micropolyps are exposed to destruction and crushing during tissue preparation (20). Besides, endometritis might be localized, which enables better detection and evaluation using hysteroscopic guided biopsies (21). Also, tissue preparation may affect the detection of plasma cells leading to missed diagnosis (22). Earlier studies confirmed the superiority of immunohistochemistry in the diagnosis of endometritis over traditional H&E stain (8, 12).

Strength and limitations of the study

The role of hysteroscopy was highlighted as a diagnostic tool. We used a diagnostic marker of high accuracy (CD138) to diagnose inflammation. However, The small sample size of our study was apparent, and maybe the etiology of some contradicting results.

Conclusion

Endometritis occurs remarkably after surgical termination of first-trimester abortion. Hysteroscopic guided biopsy followed by immunohistochemistry was associated with high diagnostic accuracy for endometritis.

Conflict of interest: None.

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Table I: Distribution of demographic data of the studied groups.

	Medical evacuation (N= 50)	Surgical evacuation (N=50)	P value
Age (years) (median, range)	30.00 (25.75-38.00)	28.00 (23.00-35.25)	0.235
Gravidity (median, range)	4.00 (3.00-5.00)	3.00 (2.00-6.00)	0.930
Parity (median, range)	3.00 (2.00-3.25)	2.00 (1.00-4.00)	0.131
Rural residence N (%)	36 (72.0%)	35 (70.0%)	0.826
Urban residence N (%)	14 (28.0%)	15 (30.0%)	

Table II: Comparison between group A and group B regarding H&E examination by Hysteroscopy and Pipelle and Immunostain examination by Hysteroscopy and Pipelle

		Group A	Group B	P-value
		N (%)	N (%)	
H&E examination by hysteroscopy	**-ve**	43 (86%)	36 (72%)	0.086
	+ve (Endometritis)	7 (14%)	14 (28%)	
H&E examination by Pipelle	**-ve**	46 (92%)	40 (80%)	0.084
	+ve (Endometritis)	4 (8%)	10 (20%)	
Immunostain examination by hysteroscopy	**-ve**	40 (80%)	30 (60%)	**0.029**
	+ve (Endometritis)	10 (20%)	20 (40%)	
Immunostain examination by Pipelle	**-ve**	44 (88%)	38 (76%)	0.118
	+ve (Endometritis)	6 (12%)	12 (24%)	

Table III: Diagnostic accuracy of the different methods used

	Sensitivity	Specificity	-VE prediction	+VE prediction	Accuracy	Likelihood Ratio	
						Value	P-value
H&E examination By Hysteroscopy	28.00	86.00	66.7	54.4	58.21%	3.00	0.083
Immunostain examination by Hysteroscopy	40.00	80.00	66.7	57.1	63.14%	4.83	**0.028**
H&E examination by Pipelle	20.00	92.00	71.4	53.5	56.40%	3.076	0.079
Immunostain examination by Pipelle	24.00	88.00	66.7	53.7	56.39	2.47	0.115