Outcome of pregnancies after cold-knife conization of the uterine cervix during pregnancy

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Summary

Objective: To determine the incidence of cervical intraepithelial neoplasia (CIN) in pregnancy and to determine the outcome of pregnancies in women treated by cold knife conization during pregnancy.

Methods: The authors retrospectively studied the cases of 19,807 pregnant patients, who presented to the 1st. Department of Obstetrics and Gynecology Semmelweis University Faculty of Medicine between January 1, 1993 and December 31, 1997. Of these, there were 1,513 spontaneous abortions, 6,170 artificial abortions and 12,124 deliveries. Cytological evidence of a high-grade squamous intraepithelial lesion (LGSIL) was found in 48 pregnant patients. A low-grade squamous intraepithelial lesion (LGSIL) was found in 55 pregnant patients. All pregnant patients with HGSIL including those with satisfactory and nonsatisfactory colposcopical examinations underwent diagnostic cold knife conization during pregnancy in the second trimester. A gynecologic pathologist (Dr. Zs. Csapó) reviewed the histopathological sections.

Results: Overall, 44 patients had CIN, three patients had microinvasive carcinoma (FIGO stage I/A1), and one patient had neither CIN nor invasive carcinoma in the HGSIL group. Among the 48 pregnant patients with HGSIL, there were two spontaneous abortions occurring during the 21st and the 22nd gestational weeks respectively, so the pregnancy loss rate was 4.2%. Forty patients (83%) delivered at term and six patients (12.5%) at preterm. Twenty-four patients (52%) delivered vaginally and 22 (48%) by cesarean section. Comparing this data with the control group consisting of pregnant patients who had LGSIL, the difference between the two group as regards the total number of adverse pregnancy outcome cases was not significant. In the three patients with microinvasive cervical carcinoma (FIGO stage I/A1), elctive cesarean section was performed, followed by an immediate abdominal hysterectomy at term.

Conclusion: The incidence of CIN in pregnancy was 0.22%. The incidence of microinvasive cervical carcinoma was 0.015%. Pregnant patients with CIN who underwent cold knife conization during pregnancy were not at increased risk of adverse pregnancy outcome, however they were at increased risk of cesarean delivery.

Key words: Cold-knife conisation; Uterine cervix; Pregnancy.

Introduction

Worldwide, cervical cancer is recognized as the second most common cancer in women, second only to breast cancer. If detected and treated early, survival rates are high. The incidence of cervical carcinoma during pregnancy varies between 0.02% and 0.05% [1-4]. The incidence of cervical intraepithelial neoplasia (CIN) in pregnancy is markedly higher, approximately 0.1-0.6% [2]. Over the last 20 years, the incidence of CIN has increased and this increase has been markedly pronounced in the younger patient population [5]. This increase is thought to be due to a concomitant increase in human papilloma virus (HPV) infection and improved screening tools [5-7]. Age-specific incidence rates of CIN are highest for women aged 15-44 years with a peak of 200 cases per 100,000 in women aged 25 [8]. Many women with CIN have not reached their desired family size. These women want to complete a current pregnancy or delay definitive treatment until the births of one or more children.

Since most patients with LGSIL have lesions that will spontaneously regress, the authors observed these pregnant patients without performing diagnostic conization during pregnancy, although the proportion of patients who have HGSIL when biopsied for LGSIL cytology, is considered approximately 5% [9-11]. If LGSIL persists throughout the entire pregnancy, a diagnostic procedure is indicated after delivery. However, all pregnant patients with cytological evidence of HGSIL with both satisfactory and nonsatisfactory colposcopic examinations were referred for diagnostic cold knife cone biopsy, even though it is not routinely performed in the US [12].

In the US, patients found to have HGSIL during pregnancy undergo colposcopy and many of them should have biopsies, but if the transformation zone is seen and the biopsy explains the HGSIL cytology, conization should be deferred until after delivery [12].

In addition in the US, conization during pregnancy should only be indicated in those patients with unsatisfactory colposcopy or microinvasive cancer found by colpo-biopsy [12].

At the 1st Department of Obstetrics and Gynecology of the Semmelweis University Faculty of Medicine, cold-knife conization has been the preferred procedure since 1981.

Despite the increase in CIN detection, few studies have assessed the effects of CIN in pregnancy, or the impact of its treatment on a current pregnancy and the outcome of the pregnancy. Consequently, clinicians have limited data on the outcomes of pregnancies subsequent to CIN diagnosis and treatment with which they could counsel patients diagnosed with CIN during pregnancy.

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The purpose of this study was to determine the incidence of CIN in pregnancy and compare the outcome of pregnancies in which cold knife conization was employed with those pregnancies where it was not employed because of LGSIL cytology.

Materials and Methods

The authors retrospectively studied the cases of 19,807 pregnant patients who presented to the 1st Department of Obstetrics and Gynecology of the Semmelweis University Faculty of Medicine between January 1, 1993 and December 31, 1997.

Of these, there were 12,124 deliveries, 6,170 artificial abortions, and 1,513 spontaneous abortions. Both cytology and colposcopy were performed in each pregnant patient. The Pap smear was taken during the first 12 weeks of pregnancy as part of antenatal care. The total number of pregnant patients with LGSIL was 55. The total number of pregnant patients with HGSIL was 48. All 48 pregnant patients with cytological evidence of HGSIL, including those with both satisfatory and nonsatisfactory colposcopical examinations, underwent diagnostic cold-knife conization. Fifteen pregnant women of the 48, who were referred for persistent cytological atypia (HGSIL) after the first conization, underwent reconization. We repeated the Pap smear four weeks after the first conization. Since the first smear was taken during the first 12 weeks of pregnancy, a diagnostic cold-knife cone biopsy was performed in the second trimester in all cases.

The procedure was performed under general anaesthesia. Normal ultrasonography was also part of the preoperative examination. A gynecologic pathologist (Dr. Zs. Csapó) reviewed the histopathological sections, including an evaluation of the internal cone margins. The average size of the removed cones was 1.5 cm.

A detailed description of the cold-knife conization follows: First, the lesion was outlined by using Schiller's iodine solution while the cervix was in traction. Then a circular incision was made involving the outer part of the cervical canal. Finally the cone of tissue was removed en bloc. We did not use Pitressin when the conization was done during pregnancy. After removing the cone of tissue, interrupted sutures were placed symmetrically into the opposite lips of the cervix.

Results

We identified 44 CIN cases between 1993 and 1998. The mean age of the 44 patients with CIN was 29 years, the median age (range) was 28 (19-41) years old and most patients were multiparous (Table 1). Three patients had microinvasive carcinoma and each of them had an adequate colposcopy.

The incidence of CIN in pregnancy was 0.22% and the incidence of invasive cervical carcinoma in pregnancy was 0.015%.

In the HGSIL group, two spontaneous abortions occurred during the 21st and 22nd gestional weeks respectively, so the pregnancy loss rate was 4.2% (Table 2).

Forty patients (83%) delivered at term and six patients (12.5%) delivered preterm. The total number of cases with adverse pregnancy outcome in the HGSIL group was thus eight, 16.7% (12.5%+4.2%) (Table 2).

The route of delivery was cesarean section in 22 patients (48%) and vaginal delivery in 24 patients (52%) (Table 2).

Table 1. — *Comparison of patient charcteristics between the two study groups (n=103).*

	HGSIL group (n=48)	LGSIL group (n=55)
Age (Mean)	29.52	27.45
<20	1	2
21-25	19	22
26-30	12	17
31-35	8	8
36-40	7	4
>40	1	2
Previous treatment		
No	33	-
Yes	15	-
Parity		
Primipara	31	40
Multipara	17	15
Colposcopical findings		
Negative	4	44
Low-grade (CIN I)	11	6
High-grade (CIN II-III)	30	-
Uncertain	3	5
Invasion	-	-

Table 2. — *Comparison of complications and pregnancy outcome between the two study groups (n=103). Values are given as %. Statistical analysis was undertaken using the $\chi 2$ test.*

	HGSIL group (n=48)	LGSIL group (n=55)	p
Abortions	2 (4.2%)	2 (3.6%)	NS
Preterm deliveries	6 (12.5%)	5 (9.1%)	NS
Total number of adverse pregnancy outcomes	8 (16.7%)	7 (12.7%)	NS
Vaginal deliveries	24 (52%)	46 (84%)	p < 0.00028
		RR 0.6 (CI 95%, 0.44-0.81)	
Cesarean section	22 (4 8%)	9 (16%)	p < 0.0012
		RR 2.8 (CI 95%, 1.43-5.48)	
Bleeding	1 (2%)		
Fever	-		

CIN or invasive carcinoma was verified in 47 cases out of the 48 patients in whom conization was performed, based on a positive screening test, with a false positive rate of 2%.

Postoperative bleeding occurred in one patient (Table 2).

In the LGSIL group (55 patients), two mid-trimester abortions occurred during the 16th and 21st gestational weeks (3.6%), and there were five preterm deliveries (9.1%).

Therefore the total number of adverse pregnancy outcomes was 12.7%. The mode of delivery in this group was vaginal delivery in 46 patients (84%) and cesarean section in nine patients (16%).

Discussion and conclusion

In the early 20st century, the number one cause of cancer deaths among women was carcinoma of the cervix. With the advent of mass screening using the Pap smear, the death rate from cervical cancer greatly declined [13]. This promising trend has recently changed with

mortality now showing a rising trend. Even the incidence of cervical carcinoma appears to be increasing in some European countries [14]. These changes are associated with a notable increase in the number of pre-invasive lesions of the cervix (CIN), along with a drop in the average age of the patients [15].

The estimated risk of progression of CIN-I to invasive carcinoma if left untreated, is less than 1%. However, this ratio is approximately 12% in regards to CIN-III [9-11]. The median transition time for the progression of CIN-I to CIN-III is approximately 58 months [11]. The median transit time for CIN-III to invasive carcinoma is approximately ten years. Currently, it is not possible to determine by any method which lesions will ultimately stabilize, regress, or progress [9-11].

Coppelson and Reid have postulated that malignant transformation of the cervix is most likely to occur when the epithelium is actively undergoing squamous metaplasia, such as in early adolescence or pregnancy [16]. Carcinoma of the cervix occurs approximately once in every 2,000 to 5,000 pregnant women, so the incidence is between approximately 0.02% and 0.05% [1-4]. The incidence of invasive cervical carcinoma during pregnancy in this study was 0.015%.

A Pap smear is a part of routine antenatal care and it is recommended during the first 12 weeks of pregnancy.

According to our practice, pregnant patients with cytological evidence of HGSIL with either a satisfactory or non-satisfactory colposcopical examination need a diagnostic procedure, since the possibility of invasive cervical carcinoma can not be excluded based on cytology and colposcopical examination.

In the US, for cases of HGSIL with satisfactory colposcopy, when the whole lesion is seen by colposcopy, biopsy is recommended. The next step following biopsy is usually a local destructive method such as cryosurgery or laser ablation, or an excisional method such as conization or the loop electrosurgical excision procedure [12]. Diagnostic conization is only performed in patients with suspicion of (micro) invasive cancer on cytology or biopsy and for lesions extending into the cervical canal and not completely seen by colposcope. The extent of destruction greatly affects the structure and function of the cervix and might affect the outcome of the pregnancy.

Although the cold-knife technique is not the standard procedure today for conization, at the 1st Department of Obstetrics and Gynecology, Semmelweis University Faculty of Medicine, the authors have performed cold-knife conization in pregnancy as a diagnostic method based on tradition. During the operation membranes were not perforated, however, it is noteworthy that four of the six preterm deliveries began with premature rupture of the membranes 4-6 weeks after the conization. This could be indicative of membrane perforation during the healing process. In contrast to other data, we found no association between the conization procedure or an adverse pregnancy outcome [8, 17,18]. Cervical incompetence occurred in two cases following the conization performed during pregnancy making the pregnancy loss rate 4.2%, which some would say is too high. Both abortions occurred two weeks following the cold-knife conization and were secondary to infection.

Our data showed a slightly higher proportion of premature births among patients receiving conization (12.5%). Most cases (10/12) of preterm deliveries were due to cervical infection (83.3%). The rate of preterm deliveries following conization in pregnancy has a wide range variability, however, in an extensive review of the literature we did not find any study in which the reconization rate was as high as it was in this study during pregnancy [8, 17, 18].

The total number of adverse pregnancy outcomes was thus eight (16.7%) which seems slightly high, but if we compare this data to a control group, a comparable pregnancy loss rate and adverse pregnancy outcome were observed. The control group was created by pregnant patients who had LGSIL (55 patients) and had not undergone conization during pregnancy. Among these 55 patients with LGSIL, there were two mid-trimester spontaneous abortions (3.6%) and five preterm deliveries (9.1%). However, the rate of cesarean delivery in the control group was only 16%.

When compared to other studies, our data showed a significant increased risk of cesarean section delivery among women with CIN who had conization during pregnancy [8, 17, 18]. This increased risk of cesarean delivery was partially caused by obstetric complications, most commonly cervical dystocia from scarring and partially by the phsysician's preference.

Pregnant patients who had conizations were more likely to have prolonged labor compared with those who did not. Considering the extraordinarily high reconization rate in our study the physician's preference was well-established.

This elevated reconization rate was well explained by the fact that all of these pregnant patients were referred from community hospitals where the first conization was not always done as extensively as it should have been. When analyzing the group of patients who had reconization (15/48), the risk of abortions and preterm labor was not higher compared to those patients who had one conization during pregnancy. Also spontaneous abortion did not occur and the rate of preterm deliveries was 13.3%.

Conization during pregnancy subjects the mother and fetus to increased risk of complications, however we experienced bleeding in only one patient (2%).

In cases of microinvasive cervical carcinoma, treatment was delayed until the fetus had matured. Cesarean section was then performed at term followed by an immediate abdominal hysterectomy.

Little data has been published about pregnancy outcome after other diagnostic methods for cervical abnormalities. According to von Rooijen and Persson there is no relationship between laser vaporization and adverse pregnancy outcome [19]. They concluded that laser vaporization of the uterine cervix before pregnancy

does not influence the outcome of a subsequent pregnancy [19]. When comparing cold-knife conization with the loop electrosurgical excision procedure (LEEP), although the depth of the cone specimens is usually less in the LEEP group than in the cold-knife group causing a slightly higher proportion of residual disease, both perioperative complications and hospitalization time are less in cases of LEEP [20, 21].

The most important limitation in this study was the small sample size. However, we conclude that conization during pregnancy is an appropriate and safe diagnostic method in cases of HGSIL. Furthermore even if invasion can not be ruled out based on the histology of the first conization, it can be repeated without jeopardizing the pregnancy.

The most important finding of this study is that women with CIN who had cone biopsy were at no increased risk of an adverse pregnancy outcome, but were at an increased risk of cesarean delivery.

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