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The Effect of Delivery on Regression of Abnormal Cervical Cytologic Findings

T. Strinić[1], D. Buković[2], D. Karelović[1], L. Bojić[3] and I. Stipić[3]

[1] Department of Obstetrics and Gynecology, University Hospital »Split«, Split, Croatia
[2] Department of Obstetrics and Gynecology, University Hospital Center »Zagreb«, Zagreb, Croatia
[3] School of Medicine, University of Split, Split, Croatia

A B S T R A C T

The purpose of this study was to determine whether abnormal antepartum cervical cytologic findings result in differing postpartum regression rates. Between 1993 and 2000, 107 pregnant women with antepartum abnormal cervical cytologic findings were identified. Papanicolaou smear data were separated into three groups by use of the CIN classification system. Postpartum regression rates of antepartum Papanicolaou smears were analyzed six months after delivery. Normalization of Papanicolaou smears in the postpartum period were observed in 50 of 107 women (46.7%). Regression of cervical cytologic findings was noted in 61 of 107 women (57%). Respectively, persistence of Papanicolaou smear was noted in 43 of 107 patients (40%). Only 3 of 107 (3%) antepartum findings progressed after delivery. Desquamation of the cervical epithelium or enhancement of a localized reparative immunologic response after vaginal delivery could play an important role in the spontaneous regression of cervical dysplasia in the postpartum period.

Introduction

Worldwide, cervical cancer continues to be an important cause of morbidity and mortality. While the refinement of cytologic screening techniques and programs for early detection have been associated with a decreasing risk of invasive disease, diagnostic and management problems associated with precursor lesions have become more important. After considering the relevant literature since 1950, Ostor concluded that the probability of cervical intraepithelial lesions becoming invasive increases with the severity of the atypia, progression to invasion

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does not always occur, and even the higher degrees of atypia may regress[1]. After considering many series with varying degrees of follow-up, he quotes approximate rates of regression as being 57% for cervical intraepithelial neoplasia (CIN) I, 43% for CIN II, and 32% for CIN III. The rates of progression to invasive cancer are thought to be 1%, 5%, and 12%, respectively[1].

The reported incidence of abnormal cervical cytology during pregnancy varies considerably, depending on risk factors of the screened population[2]. Abitbol and coworkers, in a retrospective review of 13,000 pregnant patients, reported an incidence of abnormal cervical smears of 2.2%, and, Lurain and associates reported an incidence of 1.3%[3,4]. The risk of carcinoma in situ (CIS) in pregnancy is lower, with an incidence as low as 0.025%; however, in a review, Hacker and colleagues reported a prevalence for CIS of 1.3 in 1,000 pregnancies, suggesting a trend toward an increased incidence[3–6]. Prospective evaluations of pregnant women using abrasive cytology indicates a 1.8% risk of abnormal smears, and an 8.5% risk in a university population[7,8]. Additionally, the incidence of human papilloma virus associated cytologic abnormalities discovered during pregnancy may be as high as 28%[9–11].

Pregnancy represents an ideal time to screen for cervical cancer because most women receive prenatal care. The safety, acceptance and routine use of antenatal cervical cytologic screening is responsible for increasing the number of abnormal cervical smears.

Some authors describe pregnancy as having no effect on CIN, whereas others have reported higher regression rates of cervical dysplasia in the postpartum period compared with spontaneous regression rates of dysplasia for nonpregnant women[12–14].

The objective of this study is to determine whether abnormal antepartum cervical cytologic findings result in differing postpartum regression rates.

Subjects and Methods

Between 1993 and 2000, 107 subjects were recruited from pregnant women undergoing regular checkups, with abnormal cervical cytologic findings after their initial antepartum visit. The subjects were identified through clinic and cytologic data, and they were prospectively followed cytologically and colposcopically during pregnancy and six months after delivery. All patients signed an informed consent form before acceptance into the study. Data were collected for age, gravidity, parity, smoking history, history of sexually transmitted diseases, cervical cytologic findings, colposcopic evaluation, postpartum biopsies and postpartum treatment. All patients underwent a Papanicolaou test using a spatula and cotton-tipped swab.

The terminology for cytologic findings were adjusted to the CIN (cervical intraepithelial neoplasia) classification system[15]. The initial antepartum cytologic data were separated into three groups: mild dysplasia was classified as CIN I, moderate dysplasia as CIN II, and severe dysplasia and carcinoma in situ as CIN III[15–16]. CIN I was classified as low-grade disease, but CIN II and CIN III were classified as high-grade disease[15–16]. The indications for colposcopy were CIN II and CIN III (high grade disease). In the event of abnormal cervical cytologic findings, Papanicolaou tests were repeated every 3 months during the antepartum period, and six months after delivery. A colposcopy was repeated in 2 or 3 months if the transformation zone was not fully visualized. All women delivered vaginally. Postpartum evaluation consisted of a Papanicolaou smear for all women six months

after delivery. Colposcopy and biopsy were performed in cases with Papanicolaou test CIN II or CIN III. Finally, antepartum and postpartum cervical cytologic findings were compared.

Statistical analysis was performed using Statistics for Windows (Stat Soft Inc, USA, Version 6.0). All data were analyzed using a descriptive analysis. Chi-square analyzing was used to compare CIN value in pregnancy and after delivery. Findings with an error probability value of < 0.05 were considered to be statistically significant.

Results

In the study interval, 107 pregnant women underwent cervical cytologic examination. The age of the group of women undergoing examination ranged from 22 to 37 years with a mean of 28.6 years (6.1 years), and parity median was 2. 23% were smokers, and 7% had a history of *Chlamydia trachomatis*.

Table 1. depicts antepartum and postpartum cervical cytologic findings; noticeably are the regression and persistence rates of CIN I, CIN II and CIN III in the postpartum period. Normalization of Papanicolaou smears in the postpartum period were observed in 46 (62.2%) women with antepartum finding CIN I, 2 (9.5%) patients with antepartum finding CIN II, and in 2 (16.7%) women with antepartum finding CIN III (Table 1). It is interesting that total of 50 (46.7%) antepartum abnormal Papanicolaou smears became normal post partum. Total cytologic regression was noted in 61 of 107 women (57%). Persistence of the antepartum findings were observed in 26 (35.1%) patients with CIN I, 12 (57.1%) with CIN II, and 5 (41.6%) women with CIN III in the postpartum period. Cytological findings in Papanicolaou smears after delivery was not changed in 43 (40%) of 107 patients (CIN I in 26, CIN II in 12 and CIN III in 5 women), compared to findings during pregnancy (Table 1). Only 3 (3%)

TABLE 1
PAPANICOLAOU SMEARS IN PREGNANCY AND AFTER DELIVERY

Cytological findings in pregnancy	Cytological findings after delivery				Total
	Negative	CIN I	CIN II	CIN III	
CIN I	46 (62.2%)	26 (35.1%)	2 (2.7%)	–	74 (69.2%)
CIN II	2 (9.5%)	6 (28.6%)	12 (57.1%)	1 (4.8%)	21 (19.6%)
CIN III	2 (16.7%)	2 (16.7%)	3 (25.0%)	5 (41.6%)	12 (11.2%)
Total	50 (46.7%)	34 (31.8%)	17 (15.9%)	6 (5.6%)	107 (100%)

TABLE 2
RELATION BETWEEN CIN VALUE IN PREGNANCY AND AFTER DELIVERY

	Cytological findings		p-value*
	In pregnancy N (%)	After delivery N (%)	
CIN I	74 (69.2)	34 (31.8)	0.0016
CIN II	21 (19.6)	17 (15.9)	0.5498
CIN III	12 (11.2)	6 (5.6)	0.1743

* test

TABLE 3
CYTOLOGICAL AND PATHOHISTOLOGICAL FINDINGS AFTER DELIVERY

Cytological findings	Pathohistological findings					Total
	Benign findings	Mild CIN I	Moderate CIN II	Severe CIN III	In situ carcinoma CIS – CIN III	
CIN I	–	–	–	–	–	–
CIN II	1	3	8	1	–	13
CIN III	–	–	1	5	2	8
Total	1	3	9	6	2	21

antepartum cytologic findings progressed after delivery: two CIN I to CIN II, and one CIN II to CIN III (Table 1). Comparing antepartum and postpartum cervical cytologic findings, significant regression of CIN I ($p = 0.0016$), but not CIN II and CIN III (Table 2) was seen. Cytologic progression to invasive cervical cancer was not observed. Finally, 21 (19.6%) postpartum patients underwent colposcopic examination and cervical biopsy because of CIN II and CIN III Papanicolaou test. Six cases of CIN III were found on pathologic examination (Table 3). »Cold knife« conization were performed in these six patients.

Discussion

Recent studies have shown that eradication of cervical cancer is an unrealistic goal, and that maximal safety from the cancer after a negative smear is approximately 90%, which remains roughly the same during several years after the test[17]. An organized surveillance program consists of several essential elements, including high follow-up rates, quality control of cervical cytology, and referral of confirmed cases for adequate treatment. These elements allow for quality control, monitoring of the process and evaluation of outcome. Epidemiologic studies of CIN during pregnancy have exhibited varying outcomes[11,13,14]. Many colposcopists believe that a cytology test result of high-grade disease (CIN II, III) in a pregnant patient requires special consideration. Pregnancy accentuates both normal and abnormal colposcopic findings, and clinicians may not obtain appropriate cervical biopsies out of concern of increased bleeding[12,18]. Although cervical biopsy during pregnancy is associated with an increased risk of minor bleeding, it has not been associated with increased rates of major bleeding or pregnancy loss in large studies, and a failure to perform cervical biopsies in pregnant women has been associated with missed cancers[19]. Because of the risk of potential injury to the fetus, endocervical sampling is proscribed during pregnancy. However, many authors believe CIN is not accelerated by pregnancy. In fact, cervical dysplasia often regresses completely in the postpartum period[12,13]. In a study by Hall and Walton, spontaneous regression rates for cervical dysplasia in nonpregnant women were reported as 62%, 33%, and 19% for mild, moderate and severe dysplasia, respectively[20]. Studies on regression rates of dysplasia during pregnancy have found higher regression rates in the postpartum period compared with rates in nonpregnant women[13,14,18].

A purpose of this study was to determine whether abnormal antepartum cervical cytologic findings result in differing postpartum regression rates. In this stu-

dy, 107 pregnant women were originally identified with abnormal antepartum cer -vical cytologic findings. A follow-up postpartum period of six months was chosen because it has been suggested by many authors[2–6,12–14] that this period is enough for *development of cytologic finding* of cervical dysplasia. In addition, it is standard to repeat evaluation of the dysplasia 6 months after delivery. In our study the overall postpartum regression rate for women with dysplasia was 57% (61 of 107 women). Others reported spontaneous regression rates of 30% to 54% in pregnancy[12–14,18,21–26]. Also, 50 of 107 (46.7%) antepartum abnormal Papanicolaou smears became normal postpartum. There is good agreement between our results and those of others[21–26]. Therefore our study supports these previous studies and the clinical observation that the spontaneous regression of cervical dysplasia occurs with increased frequency in the postpartum period. There was minimal progression of the antepartum Papanicolaou smears in only 3 (3%) patients.

On the basis of these observations, perhaps factors associated with parturition could be implicated. Desquamation of the cervical epithelium or enhancement of a localized reparative immunologic response after vaginal delivery could play an important role in the spontaneous regression of cervical dysplasia in the postpartum period.

To further answer this question it would be optimal to follow up a cohort of patients prospectively during pregnancy, including immunohistochemical analysis.

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T. Strinić

Department of Obstetrics and Gynecology, University Hospital »Split«, Spinčićeva 1, 21000 Split, Croatia

UTJECAJ PORODA NA POBOLJŠANJE NENORMALNIH CERVIKALNIH CITOLOŠKIH NALAZA

S A Ž E T A K

Cilj istraživanja bio je odrediti nenormalne cervikalne citološke nalaze tijekom trudnoće i ispitati njihovo mijenjanje poslije poroda. Između 1993. i 2000. godine praćeno je 107 trudnica s nenormalnim cervikalnim citološkim nalazima. Papanikolaou testovi podijeljeni su u tri skupine prema CIN klasifikaciji. Analizirano je njihovo poboljšanje šest mjeseci poslije poroda. Normalizacija Papanikolaou nalaza u razdoblju poslije poroda uočena je u 50 od 107 žena (46.7%). Poboljšanje cervikalnih citoloških nalaza nađena je u 61 od 107 žena (57%). Nalazi Papanikolaou testova nisu se promijenili u 43 od 107 ispitanica (40%). Samo 3 od 107 (3%) nenormalnih nalaza tijekom trudnoće pogoršalo se poslije poroda. Ljuštenje cervikalnog epitela ili poboljšanje lokalnog imunološkog sustava poslije poroda možebitno ima važnu ulogu u spontanoj regresiji cervikalne displazije u razdoblju poslije poroda.