Low-grade cervical squamous intraepithelial lesion during pregnancy: Conservative antepartum management

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Summary

The purpose of this retrospective study was to determine the regression rate and management of low-grade squamous intraepithelial lesions (LSIL) in pregnancy. Seventy-four women with cytological findings of LSIL were analysed during the pregnant-puerperal period (until 12 months postpartum). Age, parity, cytological and colposcopic findings, route of delivery, and postpartum follow-up were studied. The age and parity of patients ranged (average) from 12 to 32 years (21.2 ± 4.9), 0-5 (0.89 ± 1.14), and 9-32 years (16.1 ± 3.5), respectively. Thirty-nine of 55 (70.9%) and 12 of 19 (63.1%) pregnant women had normal cytology after vaginal delivery and caesarean section, respectively ($p > 0.05$). In postpartum, eight patients (10.8%) persisted with LSIL and ten (13.5%) presented high-grade squamous intraepithelial lesions. No case of unsatisfactory colposcopy and invasive carcinoma were found. LSIL during pregnancy has a high rate of regression, regardless of the route of delivery. Conservative management with colposcopic evaluation is proposed during gestation.

Key words: Pregnancy; Low-grade squamous intraepithelial lesion; Delivery; Biopsy.

Introduction

Abnormal cervical cytology in pregnancy is a common finding. Over the years, an increasing incidence of cervical intraepithelial neoplasia (CIN) has been observed [1-3], with complicating results in up to 5% of pregnancies [4]. During pregnancy, the most common cervical abnormalities are classified as low-grade squamous intraepithelial lesions (LSIL) [4-7].

Conservative management of high-grade squamous intraepithelial lesion (HSIL) was proposed with colposcopic and/or colposcopically directed biopsy evaluation during gestation [8]. This procedure has been proven to be a safe and reliable method in this condition [4-8]. Nonetheless, the management of LSIL during pregnancy is still controversial. Colposcopically directed biopsies have been recommended during pregnancy due to high persistence of CIN [4]. Others recommended small loop biopsies only in suspicious cases of possible microinvasion [9]. Moreover, little is known about the progression/regression rate of LSIL during gestation. The regression rate in returning to normal of HSIL ranged from 12% [5, 6] to 53.5% [10]. The progression/regression rate of CIN occurred, apparently, in 5.1% and 35.9%, respectively [9]. Nevertheless, a study based on pre- and postpartum histology showed a regression of 61.5% and progression to HSIL of 38.5% [11].

It is recognised that LSIL in pregnancy is controversial. The issue that continues to confront clinicians is whether LSIL should be treated. Our aim is to contribute to this debate. Thus, the purpose of this study was to determine the progression/regression rate and to analyse the clinical management of LSIL during pregnancy.

Methods

Patients

A retrospective study was conducted at FMTM from 1993 to 2000, and 946 cases of LSIL were diagnosed, with 148 (15.6%) during the pregnant-puerperal period (defined until 12 months postpartum). Nonetheless, 75 pregnant women were excluded because their a delivery and/or postpartum follow-up took place in another service. In the same period, the frequency of abnormal Papanicolaou smears (LSIL and HSIL) in our service was 2.6% (1,732 of 65,739), of which 3.3% (253 of 7,581) were in pregnant women, being 105 (13.3%) of 786 and two (1.08%) of 184 cases, respectively, HSIL and invasive cervical cancer. The pregnant-puerperal period was defined as up to 12 months postpartum. The project was approved by the Research Ethics Committee.

Methods

Age, gestational age at diagnosis, parity, age at first intercourse, cytological and colposcopic findings, route of delivery, and postpartum follow-up were obtained from medical records. All cytologies were reviewed. Cytological findings were classified according to the Bethesda System [12]. Colposcopy was performed after 3% acetic acid application, the Schiller test and Bisulfite application; it was considered unsatisfactory when the squamous-columnar junction could not be seen. Colposcopic nomenclature was according to Stafl and Wilbanks [13]. Colposcopy and biopsy in prenatal evaluation were not performed in all cases of cytological findings of LSIL because they are not routine in our service.

In the postpartum treatment of LSIL and HSIL cryocautery and conization or the loop electrosurgical excision procedure

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(LEEP) were used, respectively. Small lesions, a visible squamouscolumnar junction, and desire of future gestation were the criteria for LEEP.

Statistical analysis

The chi-square test with Yates correction and Fisher's exact test were used for statistical analysis. The differences were considered significant with $p < 0.05$.

Results

A total of 74 pregnant women with cytological findings of LSIL were analysed. The cytological finding was reported during the first trimester in 13 (17.6%) women, during the second trimester in 33 (44.6%) women, and during the third trimester in 28 (37.8%) women. The age, parity and sexarch of patients ranged (average) from 12 to 32 years (21.2 ± 4.9), 0-5 (0.89 ± 1.14), and 9-32 years (16.1 ± 3.5), respectively.

Cytological evaluation in pre- and postpartum

Of the total 74 pregnant women with a cytological diagnosis of LSIL, 51 (68.9%) had normal cytology in postpartum, of those 39 and 12 after vaginal delivery and caesarean section, respectively. In postpartum, eight patients (10.8%) persisted with LSIL and ten (13.5%) presented HSIL (Table 1).

Table 1. — *Distribution of 74 pregnant women according to cytology pre- and postpartum.*

Cytology	Prenatal evaluation		Postpartum evaluation			
			Vaginal		Caesarean	
	n	%	n	%	n	%
Without CIN	–	–	39*	70.9	12	63.1
Ascus**	–	–	4	7.3	1	5.3
CIN I	74	100	7	12.7	1	5.3
CIN II	–	–	3	5.5	2	10.5
CIN III	–	–	3	5.5	2	10.5
Total	74	100	55	100	19	100

* p = not significant (Fisher's exact test), compared to caesarean section.
** atypical squamous cells of indeterminate significance.

Colposcopic and biopsy evaluation

In Table 2, it can be seen that white epithelium was the most common finding in pre- and postpartum colposcopic evaluation. A normal transformation zone was more frequently found in antepartum evaluation. No case of unsatisfactory colposcopy was found.

Table 2. — *Distribution of colposcopic findings in the prenatal and postpartum period.*

Colposcopic findings	Prenatal		Postpartum	
	n	%	n	%
White epithelium (WP)	13	43.4	16	44.4
Mosaic (M)	–	–	1	2.8
Punctation (P)	–	–	1	28
WP + M	1	3.3	2	5.6
WP + P	2	6.7	3	8.3
M + P	1	3.3	3	8.3
WP + M + P	–	–	1	28
NTZ*	13**	43.3	9	25
Total	30	100	36	100

* Normal transformation zone; **p = 0.09, marginally significant (Fisher's test).

Eight (88.9%) of nine biopsies were normal in prenatal evaluation. Six (27.2%) biopsies presented HSIL in postpartum evaluation (Table 3).

Table 3. — *Distribution of 31 pregnant women who underwent cervical biopsy pre- and postpartum.*

Biopsy	Prenatal evaluation		Postpartum evaluation			
			Vaginal		Caesarean	
	n	%	n	%	n	%
Without CIN	8	88.9	6*	37.5	4	66.7
CIN I	–	–	6	37.5	–	–
CIN II	1	11.1	3	18.7	–	–
CIN III	–	–	1	6.3	2	33.3
Total	9	100	16	100	6	100

Four patients were submitted to biopsy in the pre- and postpartum period, of those two underwent vaginal delivery and two caesarean section. All of them showed normal Papanicolaou smears in postpartum evaluation.
* p = not significant (Fisher's exact test) compared to caesarean section.

Postpartum treatment

All patients with LSIL were treated with cryocautery. Two and three were patients treated with conization and LEEP, respectively. No case of invasive carcinoma was found. One patient with HSIL was treated at another service.

Discussion

The frequency of abnormal Papanicolaou smears (LSIL and HSIL) in pregnant women in our service is similar in relation to other authors. Reported series reveal an incidence of cytological findings of CIN from 0.93% to 5% [4, 14, 15]. Epidemiological data such as average age, parity and sexarch were similar to those shown by other authors [3]. Although these points were not the aim of this study, we do not believe that LSIL has different epidemiological factors from HSIL.

Colposcopy evaluation during pregnancy can be performed without great difficulty at any gestational age. It is usually satisfactory due to peripheral transposition of the transformation zone of the cervix [9, 16]. We found a high number of normal transformation zone (NTZ) in antenatal and postpartum evolution of pregnant women with LSIL. This contrasts with our results of colposcopic evaluation in pregnant women with HSIL, in which no case of NTZ was found [8]. This result is difficult to explain, because the increased vascularity of the cervix during pregnancy may exaggerate the acid acetic reaction and minor changes can be misinterpreted as major changes [14] and our findings showed the opposite.

We found a high rate of regression, but it must be stressed that the diagnosis of LSIL in prenatal evaluation was only based on cytological findings. Therefore, it is possible that an over-diagnosis of LSIL may have occurred. Nonetheless, other authors have shown an overall postpartum regression rate in cytological findings between 12.5% and 57%, depending on the delivery route

[17, 18]. Based on ante- and postnatal cytological and colposcopical impressions, Paraskevaidis *et al.* [9], found a regression rate of 35.9% in cases of CIN I during pregnancy.

According to the results of our study there was a considerably high rate (83%) of regression in CIN I after delivery which was not related to the delivery route. It should be emphasised that in a few cases we utilised biopsy in prenatal evaluation, therefore, the biopsy might be excluded as a cause of regression. A possible explanation is that the regression was not attributed to the pregnancy itself, but to the loss of cervical dysplastic epithelium during vaginal delivery [9]. However, it does not explain the high regression rate in cases of caesarean section, and probably the rate of regression was not due to the trauma induced by vaginal delivery [8]. Other hypotheses such as changes in the maternal immune status after pregnancy may play a role in the spontaneous regression of CIN I [5].

The results of this study showed that from the total of 74 cases of LSIL in prenatal evaluation, ten (13.5%) cases presented HSIL in cytological postpartum evaluation, of which six (60%) were confirmed by biopsy. Despite these results, there is no evidence that LSIL progresses more rapidly during pregnancy. Besides, in no case was the diagnosis of invasive carcinoma made. Invasive cervical carcinoma occurs, mainly, in cases where HSIL is found in cytology and colposcopy and biopsy are not performed [8]. After our study, we recommend that biopsy be performed in all cases of colposcopy alterations, regardless of CIN I, II or III cytological findings.

Colposcopic and cytological surveillance of cervical lesions during pregnancy seem to be safe. Also, these procedures are facilitated because the majority of pregnant women are young and the transformation zone is seen in the periphery of the uterine cervix, consequently, colposcopy is usually satisfactory during this period [8]. Another reason that reinforces the use of biopsy in this situation is to minimise treatment interventions for CIN in pregnancy, mainly in order to avoid serious complications such as haemorrhage, preterm labour and other procedures such as LEEP or cold knife conization. Nonetheless, conization is indicated in cases in which Papanicolaou smears suggest HSIL or more severe lesions and the colposcopy is unsatisfactory [16, 19]. On the other hand, in cases in which Papanicolaou smears suggest LSIL, conization may be delayed when the colposcopy is unsatisfactory, because an invasive lesion is improbable. In this specific case, surveillance with cytology and colposcopy are proposed during gestation.

We conclude that LSIL during pregnancy has a high rate of regression in postpartum, regardless of route of delivery. Conservative antepartum management with colposcopic evaluation and biopsy, if indicated, are proposed during gestation.

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