Clinical management of cervical abnormalities during pregnancy

EMBASE and pubmed database literature searches were carried out for studies conducted from 2004 onwards on the management of cervical abnormalities during pregnancy. The following tables outline information retrieved from relevant studies.

Search terms: 'pregnancy', 'pregnant', 'cervical screening', 'cervical dysplasia', 'cervical intraepithelial neoplasia', 'cervical abnormality'

Table 1: Studies on the management of cervical dysplasia in pregnant women

Authors	Country	Type of study	Subjects	Findings
Wu et al, 2014	China	Prospective	2260 pregnant women with abnormal pap smears from a total of 27,230 pregnant women	Colposcopy and cervical biopsy performed on 369 patients and then periodically every 8-12 weeks and finally 6-12 weeks after delivery. Prenatally, 15 had microinvasive squamous carcinoma, 116 had cervicitis, 124 had CIN1, 49 had CIN2 and 65 had CIN3. Authors concluded that biopsy was not necessary for patients with initial diagnosis of CIN1. None of the patients with CIN2 on which biopsies were done, progressed to invasive cancer. 2/65 patients with CIN3 progressed to invasive cancer during pregnancy, 49% remained stable and 48% regressed to CIN2. 6-12 weeks after delivery, treatment was carried out on patients with CIN3 or microinvasion. Overall 253/369 progressed to CIN1 or above. The authors concluded that colposcopy was safe and should be performed on all pregnant women with abnormal pap smears.
Coppolillo et al, 2013	Argentina	Prospective cohort	56 pregnant women with histopathological diagnosis of CIN2,3 from colposcopic guided biopsy out of 11700 pregnant women	30/56 women with CIN2,3 included in study with remaining 26 excluded because they did not comply with treatment or complete their follow-up. Postpartum assessment by pap smear, colposcopy, biopsy and endocervical curettage of the 30 women revealed persistence in 70% of cases, progression in 13.3% and regression of 16.7%. One case of invasive carcinoma was diagnosed postpartum. Authors recommend biopsy and treatment postpartum of all patients with CIN2-3 diagnosed during pregnancy and a 2 year follow-up

Table 1: continuation

Authors	Country	Type of study	Subjects	Findings
Farzan et al, 2012	USA	Retrospective cohort	50 with antepartum ASCUS smears and post-partum smears available	High risk HPV status and postpartum Pap smear results extracted. 50% were HPV+ve, 32% HPV-ve, 18% unknown HPV status. The difference in post-partum regression rates of ASCUS pap smears between HPV+ve and HPV-ve women were not statistically significant (64% vs 75%, p=0.46)
Guijon 2010	Canada	Prospective	1182 pregnant women referred to colposcopy with abnormal pap results	332/1182 underwent colposcopy directed biopsies during pregnancy with no adverse effects except bleeding.All cervical treatments were performed postpartum. Patients followed up for 5 years. There was significant agreement between colposcopic impression and histological diagnosis (p=0.001). 174 biopsies were done for CIN2 and 3 lesions. Wedge biopsy used to diagnose 4 microinvasive carcinomas. Authors concluded that colposcopic assessment poses no risk to pregnancy and that treatment of CIN can be postponed until postpartum.
Wetta et al, 2009	UK	Retrospective	625 pregnant women with abnormal cytology	469 patients were referred with LSIL and ASC-US and 128with HSIL. Biopsy performed on 138 patients at time of initial colposcopy. 32% had no evidence of CIN and there were no cases of cervical cancer. 20/78 (25.6%) women with ASC-US and LSIL who had a biopsy were diagnosed with CIN2,3. 31/60 women with HSIL who had a biopsy were diagnosed with CIN2,3. Authors concluded that pregnant women with ASC-US or LSIL cytology rarely have CIN2,3 at initial colposcopy that warrants a cervical biopsy and that colposcopy can be deferred until 6 weeks post-partum.

Table 1: continuation

Authors	Country	Type of study	Subjects	Findings
Siddiq et al, 2006	UK	Retrospective analysis	49 pregnant women referred for colposcopy.	All women had a colposcopy at their 1st antenatal visit but only 3/49 had a biopsy because of high grade colposcopic assessments with no complications. Resulting histological diagnoses were 2 cases of CIN3 and one case of HPV. Postpartum, all 49 women were assessed colposcopically between 1-25 weeks. 1 patient was diagnosed with invasive squamous carcinoma following LLETZ. Colposcopic assessment antenatally had a 60% concordance with final histological diagnosis and 68% concordance when performed postpartum. Cytologic concordance with final histology was 58%. Authors recommended conservative management of patients during the antenatal period with 1 colposcopic assessment at the time of the index abnormal smear and 1 post-partum.
Boardman et al, 2005	US	Prospective cohort	283 pregnant women with abnormal pap smears	Patients referred for colposcopy and biopsies were obtained when deemed necessary. 67 (24%) women had ASCUS, 147 (52%) LSIL, 67 (24%) HSIL and 2 (0.7%) AGUS. The authors concluded that among those biopsied, pregnant women with ASCUS or LSIL as compared to pregnant women with HSIL, were less likely to have either antepartum or postpartum CIN2 or worse.
Kaplan et al, 2004	US	Retrospective review	129 patients with antepartum LSIL and postpartum evaluations	Patients initially diagnosed with abnormal cytology from pap smears. Colposcopy performed late in 1st trimester or early 2nd trimester and repeated every trimester. 6-8 weeks postpartum cytology and colposcopy performed. 129 patients diagnosed with LSIL antepartum. Postpartum, 62% of LSILs regressed, 32% persisted and 6% progressed to HSIL. 29 patients diagnosed with HSIL antepartum, all of which persisted postpartum and 3 (11%) found to have microinvasive squamous cell carcinoma after conization. Follow-up data showed high rates of recurrence for both LSIL and HSIL 2-5 y after diagnosis of SIL in the antepartum. Authors concluded that most cases of LSIL regressed or remained stable

				during pregnancy whereas HSIL diagnosed in the antepartum persisted in the postpartum and 11% progressed to invasive carcinoma postpartum

Search terms: 'pregnancy', 'pregnant', 'progression', 'persistence', 'natural history', 'cervical dysplasia', 'cervical intraepithelial neoplasia', 'cervical abnormality'.

Table 2: Studies on the effects of pregnancy on progression of cervical dysplasia

Authors	Country	Study type	Subjects	Methods/Findings
Cubo-Abert 2012	Spain	Retrospective cohort	80 pregnant women with abnormal cytology	Postpartum cytologic and histologic findings compared to antepartum findings. Antepartum, 40 patients had LSIL and 40 had HSIL. Postpartum, there was an overall regression rate of 45% in the LSILs and 20% in the HSILs. The regression rate in patients ≤25 years was 52.6% vs 26.2% in women >25 years. In patients with HSIL, those >25 years had twice the risk of progression or persistence than younger patients. Also HPV16+ve cases (n=21) had a regression rate of 9.5% vs 52.2% for HPV16 –ve cases (n=23).
Fader et al, 2010	US	Retrospective cohort	1079 pregnant women referred for colposcopy after abnormal cervical cytology	91 women had a biopsy of which 68% had a colposcopic impression of HSIL. There were no cases of cervical cancer. Postpartum, among women referred with either ASC (n=325) or LSIL (n=589) cytology, 64% regressed to normal, 29% had a persistent low grade abnormality and 6% had a high-grade lesion. Among women referred with HSIL (n=164), 53% regressed to normal, 16% regressed to a lower grade lesion, and 31% had a persistent high-grade dysplasia. Women with LSIL who regressed after pregnancy were more likely not to be smokers. The authors conclude that the study data support the safety and accuracy of colposcopy by experienced colposcopists andproposed that cervical biopsies in pregnancy may not be necessary unless invasive cancer is suspected.

Henes et al, 2013	Germany	Retrospective	65 pregnant women referred for colposcopy after abnormal cervical cytology	46.2% referred for Pap IIID (LSIL/HSIL), 40% for Pap IVa (HSIL/CIS), 6.2% for Pap III (ASCUS, ASC-H) or PapII (normal) with condyloma and 1 patient had Pap IVb (HSIL,CIS,Micro). Postpartum, 40% of cases were in remission, 26.2% persisted, 4.5% went into partial remission and 3% progressed. (Munich II nomenclature used in original paper – corresponding Bethesda system added according to publication by Boehmer et al, 2014. BMC Inf Dis 14:674)

Table 2: continuation

Authors	**Country**	**Study type**	**Subjects**	**Methods/Findings**
Serati et al, 2008	Italy	Prospective	78 pregnant women with abnormal pap smear referred for colposcopy.	Women with LSIL or HSIL underwent colposcopic examination by 2 trained colposcopists and women with a histological diagnosis of CIN included in prospective study. 36 women had CIN2-3, and 42 had CIN1. Post-partum colposcopic examinations carried out 8-12 weeks after delivery: among women with CIN2-3 antenatally, there were no cases of progression to microinvasive disease, 19 (53%) persistent CIN 2-3, 17 regressions to CIN1 (47% regression overall). Among women with CIN1 antenatally, 6 (14%) progressed to CIN2-3, 7 (47.3%) persisted at CIN1 and 29 regressed (69%). Authors concluded that conservative management for CIN2-3 diagnosed during pregnancy is safe in the hands of experienced colposcopists. Also that patients with CIN1 diagnosed antenatally could avoid colposcopic examination until post-partum
Frega et al, 2007	Italy	Prospective cohort	31 pregnant women with abnormal cervical cytology	10 referred with LSIL and 21 with HSIL. Histological analysis of colposcopy-directed biopsies revealed 10 cases of CIN1 (33%), 5 of CIN2 (16%) and 16 of CIN3 (51%). 22 cases were high risk HPV+ve and 9 were HPV-ve. Postpartum, 9/10 cases of CIN1 regressed and 1 progressed to CIN2; 2/5 CIN2 regressed and 3/5 persisted; 8/11 CIN3 regressed and 3/11 persisted. Authors conclude that hrHPV testing

	may be added to cytology and colposcopy to improve follow-up of pregnant patients with SIL and indicate persistence/regression postpartum.

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