Atypical Glandular Cells in Cervical Smear During Pregnancy and Postpartum Period

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The 2001 Bethesda System defines *atypical glandular cells* (AGC) as glandular cell abnormalities that are distinct from adenocarcinoma or adenocarcinoma *in situ*.¹ Before 2001, a spectrum of glandular cell abnormalities in cervical smears was grouped under *atypical glandular cells of undetermined significance* (AGUS) and defined as glandular cells exhibiting changes beyond reactive or reparative changes, but lacking unequivocal features of invasive adenocarcinoma.² The incidence and clinical significance of AGUS have been extensively reported,³⁻⁶ however, studies reporting AGUS smears in pregnancy and postpartum period are very limited.

Chhieng and colleagues⁷ have reported the largest number of AGUS smears in pregnancy and postpartum period (n=35). Among the 13,361 smears performed during the 3-year study period, this group reported a 0.26% incidence rate with a mean patient age of 29. Of the 35 patients with AGUS smears, 8 patients were lost to follow up, 17 were referred for colposcopy and biopsy, and 10 had repeated smears. For those who underwent colposcopy and biopsy, five patients had histologically proven cervical intraepithelial lesions. The others had benign pathologies including squamous cell metaplasia, endocervical or endometrial polyps, Arias-Stella reactions and microglandular hyperplasia. Two of the 10 patients had persistent abnormalities on repeated smears but their outcomes were not reported. The authors reported the incidence of significant pathology in this study as 29%. However, the incidence rate of significant pathology was calculated on the basis of the 17 cases referred for colposcopy and biopsy only, and did not include the patients being followed with repeated smears which would reduce the rate of significant pathology to less than 20%.

Two other studies have been reported on pregnancy related AGUS, although these involved smaller numbers of patients. Michael and colleagues⁸ reported 26 cases of AGUS during pregnancy or postpartum period, most of which were followed with repeated cervical smears after 3 to 6 months. Biopsies were performed in the postpartum period only if atypia persisted on repeat smears. Eight patients had colposcopy directed biopsies and only 2 patients were diagnosed with squamous cell intraepithelial lesions. Kim and colleagues⁹ reported a large study of 326 patients: 21 were diagnosed with AGUS during pregnancy or within 8 weeks postpartum. Only one of the 21 patients had significant pathology showing carcinoma *in situ*, though the method of follow-up was not specified. From the studies described above, the incidence of

significant pathology following an abnormal glandular cytology on cervical smear during pregnancy or postpartum period was not as high as has been demonstrated in the non-pregnant population (31% to 48%).^{4,10,11}

The observed lower incidence could be explained by 1) over-diagnosis of AGUS during pregnancy and postpartum period, and 2) younger age in patients having pregnancy-related AGUS smears. A number of reports have emphasized pregnancy-related cellular changes and their diagnostic pitfalls.¹³⁻¹⁷ Decidual cells, trophoblasts, and Arias-Stella reactions frequently cause confusion in the interpretation of cervical smears of pregnant patients. Distinguishing between Arias-Stella cells and cells of glandular abnormalities can be difficult because the morphologic characterization of the former is poor.¹⁷ It is therefore essential for the pathologists evaluating the smear to know the pregnancy status of the patient. Misdiagnosis could be minimized by the awareness of the physiological changes associated with pregnancy. The mean age of patients having AGUS during pregnancy or postpartum period was only available in one of the papers discussed above. The mean age of these patients was much lower (mean age=27) than in non-pregnant populations (ages 44 to 50),^{6,9,10,12} and could partially explain the lower incidence of significant pathology in pregnancy-related AGUS as the risk of malignancy is lower in younger women.

From the very limited evidence currently available, no clear guidelines for the management of atypical glandular cells detected in cervical smears during pregnancy or postpartum period can be developed. Sub-classification of atypical glandular cells into *favor neoplasia* or *not otherwise specified* as required in the 2001 Bethesda System would help the colposcopists in making clinical diagnoses.¹ Communication between pathologists and colposcopists is fundamental. Colposcopy during pregnancy is a safe procedure and colposcopy directed biopsy, in experienced hands, helps exclude significant cervical pathologies for selected cases. If malignancy is not evident from initial colposcopic evaluation, follow-up colposcopic and cytologic surveillance are acceptable methods for management during pregnancy. However, endocervical sampling is not advisable during pregnancy. Cone biopsy during pregnancy increases the risk of pre-term, pre-labor rupture of membranes and should only be performed if malignancy is highly suspicious.¹⁸ After 8 weeks postpartum, invasive investigation can safely be performed and patients should be managed according to the 2001 Bethesda consensus guidelines.¹

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