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Original Article

Postpartum Pap Smear Results in Women with Abnormal Pap Smears Detected at First Antenatal Care: A Retrospective Study in a Songklanagarind Hospital

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ABSTRACT

Objective: To assess the remission rate at postpartum periods of abnormal Pap smears during pregnancy, and to identify the demographic and clinical characteristics of pregnant women with abnormal Pap smears.

Material and Methods: Pregnant women, who had antenatal care (ANC) in Songklanagarind Hospital in period of January 2011 to December 2019, were identified retrospectively. Exclusion criteria included inaccessible results of Pap smears during pregnancy and postpartum periods. Medical records of all pregnant women with abnormal Pap smears were reviewed. The association between Pap smear results during pregnancy and postpartum were analyzed by Cramer's V statistic ranging from 0 to 1, with a 1 indicating perfect association.

Results: Of these 8,238 pregnant women had available Pap smear results, 109 (1.3%) women were shown with abnormal results. The most common of abnormality from Pap smears were atypical squamous cells of undetermined significance. In postpartum period, 50 women who had abnormal Pap smear during pregnancy, underwent postpartum follow-up examination at six weeks postpartum, respectively. The majority of results (84.0%) were normal whilst rate of remission occurred in 45 women (90.0%). The association of Pap smears between during pregnancy and postpartum was shown to have a small association (Cramer's V = 0.2).

Conclusion: There was low prevalence of abnormal Pap smear during pregnancy and high remission rate at postpartum. However, health care providers should be aware of cervical cancer screening in all pregnant women, because many women had not undergone cervical cancer screening before pregnancy.

Keywords: outcome; pap; pregnancy

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INTRODUCTION

The incidence of cervical cancer has been decreasing due to effective screening methods and appropriate management. These result in the increasing of incidence of pre-invasive diseases. This pattern is the same as in pregnant women; wherein, the incidence of pre-invasive diseases was 0.5-9.0%[1-3], and peaks in 20-30 year old women.[1] The overall risk factors of cervical cancer were not different in pregnant and non-pregnant women; however, early first sexual intercourse, multiparity as well as early diagnosis at a younger age often found in pregnant women. Nonetheless, stage and prognosis of disease were not different.[1]

During pregnancy, the physiologic changes in cervical epithelium and glands; such as squamous metaplasia and increasing mucous discharge, may interfere with investigation and interpretation of cytology and colposcopy.[2, 4] However, the immune system coupled with vaginal delivery may lead to a high risk for remission[1, 5] of the lesions during pregnancy (25.0-77.0%); with the persistence rate being 47.0-52.7% and the progression rate being 0.0-11.0%.[1, 3, 6] Treatment of abnormal Pap smears in pregnant women is presently conservative. According to the American Society for Colposcopy and Cervical Pathology (ASCCP) 2019, the diagnostic excisional procedure is advocated only in pregnant women who are suspected of invasive cancer. Follow-up with cytology or human papillomavirus (HPV) every 12 to 24 weeks is recommended in pregnant women who are diagnosed with histologic high-grade squamous intraepithelial lesions (HSIL).[7]

In pregnant women with cytology of atypical squamous cell of undetermined significance (ASC-US), or low-grade squamous intraepithelial lesions (LSIL) found in 1.6-9%, the histologic diagnosis of normal and cervical intraepithelial neoplasia (CIN) I was found in 14.7-50.0%[8, 9] whilst invasive cancer was found in only 2.2%.[8] In pregnant women with cytology of atypical squamous cell one cannot exclude HSIL (ASC-H) and HSIL was found in 0.4-0.7%.[10] The rate for those diagnosed with histologic CIN I-II was 24.2%[1], and progression was found in 7.0-14.0%.[5, 11, 12] The incidence of abnormal Pap smear in Thai pregnant women was 1.24-7.0%[13, 14, 15] and the histologic CIN II-III and cancer were 10.0% and 3.8%, respectively.[16] Hence, the objectives of this study were to assess the remission rate at the postpartum period of abnormal Pap smears during pregnancy. Additionally, this study aimed to identify the demographic and clinical characteristics of pregnant women with abnormal Pap smears.

MATERIAL AND METHODS

This retrospective study was approved by the Human Research Ethics Committee from the Faculty of Medicine, Prince of Songkla University (REC. 62-140-12-1), and was conducted from 1st July, 2019 to 31st August, 2020. In Songklanagarind Hospital, cervical cancer screening was routinely performed in pregnant women at first antenatal care (ANC). The data from pregnant women who had ANC; between January, 2011 and December, 2019; with available results of Pap smears were included to be the denominator. Women with abnormal Pap smears were retrieved as nominator for calculation the prevalence. The pregnant women who had no result of Pap smear at postpartum period were excluded and their medical records were reviewed for demographic and clinical characteristics as well as their delivery outcomes; including results of Pap smears during the postpartum period.

The demographic data of the pregnant women included: age, gravida, parity, gestational age at first ANC, serology results, sexual transmitted diseases and Pap smear results before pregnancy. The information of delivery outcomes included: gestational age, route and fetus. Pap smear results, which were reported according to the Bethesda system 2001[17] and clinical characteristics; including: HPV testing result, colposcopic examination and histological results during ANC and postpartum periods, were collected.

The sample size was calculated on an estimating finite population of 150 in a 10-year period in the study setting, and assumed an average remission rate from a previous study; which was 60.0%.[18] With an acceptable error of 15.0%, we required at least 41 pregnant women with abnormal Pap smear results to be included in the study, from the results of Pap smears during pregnancy and postpartum. The statistical analysis used program R version 4.0.2 (2020-06-22, R Foundation, Vienna, Austria).

All data were entered into the EpiData 3.1 program, and analyzed by R software version 4.0.3 (The R Foundation for Statistical Computing 2020, Vienna, Austria). All data were descriptively reported in percentage, mean (standard deviation) and range, as appropriate. The association between Pap smear results during pregnancy and postpartum were analyzed by Cramer's V statistic using "cramer V" command in r-companion package. Cramer's V ranges from 0 to 1, with a 1 indicating a perfect association.[19]

RESULTS

There were 12,958 pregnant women who had ANC in Songklanagarind Hospital, between January, 2011 and December, 2019. Pap smears were performed in 8,238 women, and the results were abnormal in 109 women. From deliveries at our hospital of 83 women, 50 women had followed up Pap smears in their postpartum period (Figure 1). The incidence of abnormal Pap smears in pregnant women was 1.3% (109/8,238).

There were 50 women who had abnormal Pap smear during pregnancy and followed up at postpartum period, the demographic and delivery data was presented in Table 1. The most abnormal result of Pap smears during pregnancy was ASC-US (62.0%), and the conventional method was used in all pregnant women. HPV testing and colposcopy were undertaken during pregnancy in 18.0% and 72.0%, respectively, and postpartum in 6.0% and 32.0%, respectively. Biopsies of the cervix during pregnancy were performed in only 3 women (6.0%), and the pathological results were no cancer reported whereas biopsy of the cervix at postpartum was conducted in 26.0%, and no cancer was reported in these pathological results. Mean follow up time of postpartum of women in this study was 2.2±2.1 years (Table 2). However, CIN III was found in 0.9% (1/109); this patient had loss of follow-up in the postpartum period.

The association of Pap smears between, during pregnancy and postpartum was shown to have a small association (Cramer's V = 0.2), as in Table 3. The remission rate was found in 90.0%. For non-remission, 3 women had persistence and 2 women had progression in their Pap smear results. There was only one pregnant woman who had CIN III, from a cervical biopsy during ANC, but she was lost to follow-up in the 6-week postpartum period. Additionally, there were 4 women who had no cervical biopsy during ANC, and had CIN III in a cervical biopsy at the postpartum period.

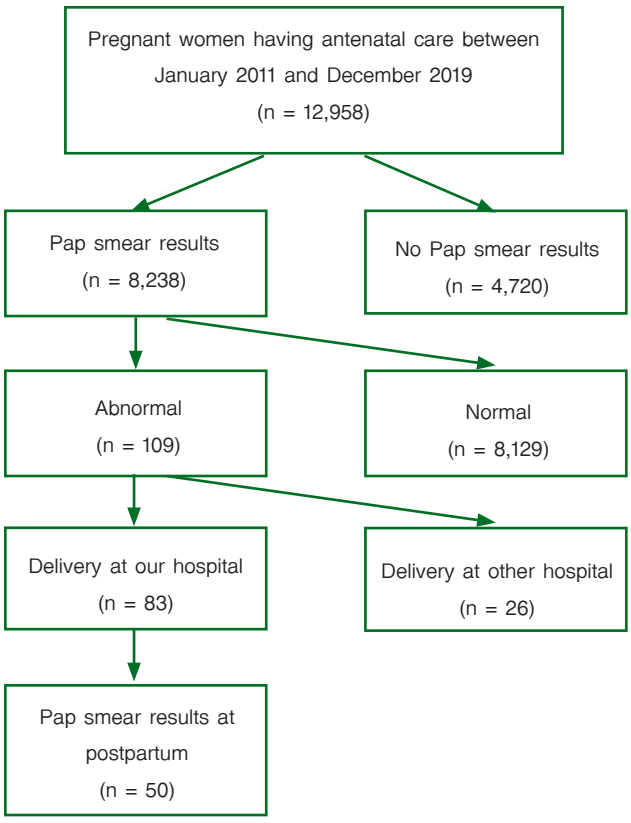

Figure 1 Pregnant woman with Pap smears

Table 1 Demographic and delivery data (N=50)

Demographic data	N	(%)
Age group (Years)		
<20	2	(4.0)
20–34	35	(70.0)
≥35	13	(26.0)
Gravida		
Primi	19	(38.0)
Multi	31	(62.0)
Parity		
Nullipara	19	(38.0)
Multipara	31	(62.0)
Gestational age at first ANC (trimester)		
First	46	(92.0)
Second	3	(6.0)
Third	1	(2.0)
Anti-HIV		
Reactive	1	(2.0)
Non-reactive	49	(98.0)
Previous Pap smear		
Normal	18	(36.0)
Not done	32	(64.0)
Previous Pap smear (year)		
Mean(S.D.)	4.1	(2.6)
Delivery		
Abortion	3	(6.0)
Preterm	3	(6.0)
Term	44	(88.0)
Route of delivery		
Vagina	32	(64.0)
Cesarean section	18	(36.0)
Indication of cesarean section		
CPD	6	(33.3)
Fail induction	1	(5.6)
Fetal distress	3	(16.7)
Prior	7	(38.9)
Breech presentation	1	(5.6)
Birth weight of fetus		
Low	4	(8.0)
Normal	40	(80.0)
No data	6	(12.0)
Gender of fetus		
Male	20	(40.0)
Female	23	(46.0)
No data	7	(14.0)

ANC = antenatal care; Anti-HIV = Anti-human immunodeficiency virus; CPD = Cephalopelvic disproportion

Table 2 The results of Pap smears during antenatal care and postpartum (N=50)

	During antenatal care	Postpartum
	N (%)	N (%)
Pap smear result		
Normal	0 (0.0)	42 (84.0)
ASC-US	31 (62.0)	6 (12.0)
ASC-H	1 (2.0)	0 (0.0)
LSIL	14 (28.0)	2 (4.0)
HSIL	2 (4.0)	0 (0.0)
AGC-NOS	1 (2.0)	0 (0.0)
AIS	1 (2.0)	0 (0.0)
HPV result		
Negative	3 (6.0)	1 (2.0)
Positive -16 18	3 (6.0)	1 (2.0)
16	3 (6.0)	1 (2.0)
Not done	41 (82.0)	47 (94.0)

Table 2 (Continued)

	During antenatal care	Postpartum
	N (%)	N (%)
Colposcopy		
Yes	36 (72.0)	16 (32.7)
No	14 (28.0)	34 (67.3)
Satisfy		
Satisfied	32 (88.9)	15 (93.8)
Unsatisfied	4 (11.1)	1 (6.2)
Impression		
Normal	9 (25.0)	5 (31.2)
LGL	22 (61.1)	8 (50.0)
HGL	5 (13.9)	3 (18.8)
Biopsy		
Yes	3 (6.0)	13 (26.0)
No	47 (94.0)	37 (74.0)
Pathological result		
Normal	2 (4.0)	5 (38.5)
CIN I	1 (20.9)	3 (23.1)
CIN II	0 (0.0)	1 (7.7)
CIN III	0 (0.0)	4 (30.8)

ASC-US = atypical squamous cells of undetermined significance; ASC-H = atypical squamous cells cannot exclude HSIL; LSIL = low-grade squamous intraepithelial lesions; HSIL = high-grade squamous intraepithelial lesions; AGC-NOS = Atypical glandular cells-not otherwise specified; AIS = Adenocarcinoma in situ; HPV = human papillomavirus; LGL = Low grade lesion; HGL = High grade lesion; CIN = cervical intraepithelial neoplasia

Table 3 The correlation of Pap smears between and during antenatal care and the postpartum period

Pap smear during ANC	Pap smear in postpartum period		
	Normal	ASC-US	LSIL
ASC-US	26	3	2
ASC-H	1	0	0
LSIL	11	3	0
HSIL	2	0	0
AGC-NOS	1	0	0
AIS	1	0	0

ASC-US = atypical squamous cells of undetermined significance; ASC-H = atypical squamous cells one cannot exclude HSIL; LSIL = low-grade squamous intraepithelial lesions; HSIL = high-grade squamous intraepithelial lesions; AGC-NOS = Atypical glandular cells-not otherwise specified; AIS = Adenocarcinoma in situ; ANC = Antenatal care

DISCUSSION

The detection rate of abnormal Pap smears during pregnancy was 1.3%, with the majority being ASC-US. Only half of the pregnant women with abnormal results followed up with Pap smears at postpartum, and the remission rate was found in 90.0%. The association of Pap smears between, during pregnancy and postpartum was shown to be small.

The rate of abnormal Pap smears in pregnant women, using the conventional Pap smear method in our study, was lower than previous studies (2.6-8.1%).[10,12-14, 18, 20] There were several explanations. First, the prevalence of abnormal Pap smears in women was lower Southern Thailand.[15] Second, abnormal Pap smears were more common in elderly women, rather than those of a reproductive age[16], whom had a higher probability of becoming pregnant. Third, the use of different methods of examination, having different diagnostic performance, would also affect the prevalence as a detection rate of abnormal results. In

another study, using a liquid-base method, this was 7.0%; which was higher than our study that used the conventional Pap smear method.[13] Our study showed that two-thirds of pregnant women who had abnormal Pap smears had never undergone a Pap smear before, and these were detected at their first ANC visit.

The most common, abnormal Pap smear result found was ASC-US/LSIL, which was consistent with the findings from previous studies.[9, 10, 18] The pregnant women were in an early reproductive age, had a short interval of HPV exposure and a high rate of eliminating HPV infection.[21] Additionally, normal physiologic changes of cervical cytology in pregnant women might result in less severity of abnormal results.[2] Only one-fifth of pregnant women with abnormal Pap smears underwent HPV testing according to the recommendation guidelines of ASCCP 2019.[7] This may be because HPV testing has only been available in our hospital since 2004, and is expensive. A high rate of colposcopy was found with regards to abnormal Pap smears. Low rate of cervical biopsies in colposcopy was shown, as the cervical biopsy and diagnostic excisional procedure was only recommended if cancer was suspected[7], and there was an awareness of the risk for preterm birth[22-24,] or spontaneous abortion.[24] However, in our study CIN II-III during pregnancy was diagnosed with invasive cervical cancer from the loop electrosurgical excision procedure in 5.4%[25] of patients and, CIN III was found in 0.9% (1/109); this patient had loss to follow-up in the postpartum period.

Most pregnant women delivered at term, with preterm delivery being found in 6.0% which was the same as a study conducted in China (9.9%).[20] The regression rate of abnormal Pap smear results at postpartum in our study (90.0%) was higher than a previous study (62.0%).[18] This may be because of higher prevalence of low grade lesions, and lower follow-up rates in our study. Previous studies showed the regression rate in low grade lesions ranging from 45.0% to 69.0%, and in high-grade lesions from 20.0% to 47.3%.[12, 26, 27] Moreover, the regression rate at postpartum was higher in women performing vaginal birth than those undergoing cesarean delivery; particularly in women with high grade lesions.[28, 29] Higher rates of CIN III, detected at postpartum, were found in our study; due to performing HPV testing, colposcopy and cervical biopsies according to the guidelines of ASCCP-2019.[7]

It was not surprising that the association between Pap smears during ANC and postpartum was small, because the physiologic changes of cervical cytology might result in ASCUS/LSIL detection at higher rates during pregnancy. Additionally, cervical and immunologic repair after vaginal delivery might result in the regression in postpartum periods.[2] There are only a few studies in Southeast Asian countries assessing abnormal Pap smears during pregnancy and postpartum. Our study emphasized the importance of follow up of abnormal Pap smears. Although, the regression rate would be high, some of them required further, more proper diagnosis and treatment.

One limitation of this study was in its retrospective data collection; wherein, postpartum Pap smears were not conducted in all pregnant women with abnormal Pap smears. In addition, some missing data on pregnant outcomes, gestational age and route of delivery data were not noted. Finally, the postpartum follow-up was performed only immediately after 6 weeks of postpartum. Postpartum follow up of abnormal Pap smears during pregnancy is important, and the methods to improve the rate of postpartum examination should be further studied.

CONCLUSION

There was low prevalence of abnormal Pap smear during pregnancy and high remission rate at postpartum. However, health care providers should be aware for cervical cancer screening in all pregnant women, because many women had not experienced cervical cancer screening before pregnancy.

CONFLICT OF INTEREST

All authors report no conflicts of interest.

REFERENCES

1. Tewari KS. Cancer in Pregnancy. In: Disaia PJ, Creasman WT, Mannel RS, Mcmeekin DS, Mutch DG, editors. Clinical Gynecologic Oncology. 9th ed. Philadelphia: Elsevier 2018; p.353-418.
2. Yang KY. Abnormal pap smear and cervical cancer in pregnancy. Clin Obstet Gynecol 2012;55:838-48.
3. Kunos CA, Abdul-Karim FW, Dizon DS, Debernardo R. Cervix uteri. In: Chi DS, Berchuck A, Dizon DS, Yashar CM, editors. Principles and Practice of Gynecologic Oncology. 7th ed. Philadelphia: Wolters Kluwer; 2017;p467-510.
4. Flannelly G. The management of women with abnormal cervical cytology in pregnancy. Best Pract Res Clin Obstet Gynaecol 2010;24:51-60.
5. Coppola A, Sorosky J, Casper R, Anderson B, Buller RE. The Clinical Course of Cervical Carcinomain SituDiagnosed during Pregnancy. Gynecol Oncol 1997;67:162-5.
6. Amant F, Ungar L. Cancer in Pregnancy. In: Berek JS, Hacker NF, editors. Berek & Hacker's Gynecologic Oncology. 6th ed. Philadelphia: Wolters Kluwer; 2015. p.692-704.
7. Perkins RB, Guido RS, Castle PE, Chelmow D, Einstein MH, Garcia F, et al. 2019 ASCCP Risk-Based Management Consensus Guidelines for Abnormal Cervical Cancer Screening Tests and Cancer Precursors. J Low Genit Tract Dis 2020; 24:102-31.
8. Broderick D, Matityahu D, Dudhbhai M, Alter S. Histologic and colposcopic correlates of ASCUS pap smears in pregnancy. J Low Genit Tract Dis 2002;6:116-9.
9. Dunn TS, Bajaj JE, Stamm CA, Beaty B. Management of the minimally abnormal papanicolaou smear in pregnancy. J Low Genit Tract Dis 2001;5:133-7.
10. Wu YM, Wang T, He Y, Song F, Wang Y, Zhu L, et al. Clinical management of cervical intraepithelial neoplasia in pregnant and postpartum women. Arch Gynecol Obstet 2014;289:1071-7.
11. Yost NP, Santoso JT, McIntire DD, Iliya FA. Postpartum regression rates of antepartum cervical intraepithelial neoplasia II and III lesions. Obstet Gynecol 1999;93:359-62.
12. Serati M, Uccella S, Laterza RM, Salvatore S, Beretta P, Riva C, et al. Natural history of cervical intraepithelial neoplasia during pregnancy. Acta Obstet Gynecol Scand. 2008;87:1296-300.
13. Khaengkhor P, Mairaing K, Suwannarurk K, Thaweekul Y, Poomtavorn Y, Pattaraarchachai J, et al. Prevalence of abnormal cervical cytology by liquid based cytology in the antenatal care clinic, Thammasat University Hospital. J Med Assoc Thai 2011;94:152-8.
14. Lertcharernrit J, Sananpanichkul P, Suknikhom W, Bhamarapravatana K, Suwannarurk K, Leaungsomnapa Y. Prev lence and Risk Assessment of Cervical Cancer Screening by Papanicolaou Smear and Visual Inspection with Acetic Acid for Pregnant Women at a Thai Provincial Hospital. Asian Pac J Cancer Prev 2016;17:4163-7.
15. Chichareon SB, Tassee S, Wootipoom V, Buhachat R, Harnprasertpong J. Situation analysis for management of abnormal Pap smears in the lower southern Thailand. Asian Pac J Cancer Prev 2005;6:286-94.
16. Kantathavorn N, Kietpeerakool C, Suprasert P, Srisomboon J, Khunamornpong S, Nimmanhaeminda K, et al. Clinical relevance of atypical squamous cells of undetermined sig nificance by the 2001 bethesda system: experience from a cervical cancer high incidence region. Asian Pac J Cancer Prev 2008;9:785-8.
17. Solomon D, Davey D, Kurman R, Moriarty A, O'Connor D, Prey M, et al. The 2001 Bethesda System: terminology for reporting results of cervical cytology. JAMA 2002;287:2114-9.
18. Kaplan KJ, Dainty LA, Dolinsky B, Rose GS, Carlson J, McHale M, et al. Prognosis and recurrence risk for patients with cervical squamous intraepithelial lesions diagnosed during pregnancy. Cancer 2004;102:228-32.
19. Mangiafico SS. Summary and Analysis of Extension Program Evaluation in R. 2016 [Monograph on the Internet] New Brunswick: Rutgers Cooperative Extension [cited 2029 November 5]. Available from: https://rcompanion.org/handbook/
20. Hong JN, Berggren EK, Campbell SL, Smith JS, Rahangdale L. Abnormal cervical cancer screening in pregnancy and preterm delivery. Paediatr Perinat Epidemiol 2014;28:297-301.
21. Erickson BK, Einstein MH, Huh WK. Preinvasive Disease of the Lower Genital Tract. In: Chi dS, Berchuck A, Dizon DS, Yashar CM, editors. Principles and Practice of Gynecologic Oncology. 7th ed. Philadelphia: Wolters Kluwer; 2017. p.114-29.
22. Kyrgiou M, Mitra A, Arbyn M, Stasinou SM, Martin-Hirsch P, Bennett P, et al. Fertility and early pregnancy outcomes after treatment for cervical intraepithelial neoplasia: systematic review and meta-analysis. BMJ 2014;349:g6192.
23. Jin G, LanLan Z, Li C, Dan Z. Pregnancy outcome following

loop electrosurgical excision procedure (LEEP) a systematic review and meta-analysis. Arch Gynecol Obstet 2014;289:85-99.

24. Bjorge T, Skare GB, Bjorge L, Trope A, Lonnberg S. Averse Pregnancy Outcomes After Treatment for Cervical Intraepithelial Neoplasia. Obstet Gynecol 2016;128:1265-73.
25. Siegler E, Lavie O, Amit A, Vaknin Z, Auslander R, Blumenfeld Z. Should the Risk of Invasive Cancer in Pregnancy and the Safety of Loop Electrosurgical Excision Procedure During the First 15 Weeks Change Our Practice? J Low Genit Tract Dis 2017;21:299-303.
26. Cubo-Abert M, Centeno-Mediavilla C, Franco-Zabala P, Merced-Vazquez C, Castellvi J, Garcia A, et al. Risk factors for progression or persistence of squamous intraepithelial lesions diagnosed during pregnancy. J Low Genit Tract Dis 2012;16:34-8.
27. Suzuki K, Furuhashi M, Kawamura T, Kubo M, Osato K, Yamawaki T. Comparing Papanicolaou test results obtained during pregnancy and post-partum. J Obstet Gynaecol Res 2017;43:705-9.
28. Ahdoot D, Van Nostrand KM, Nguyen NJ, Tewari DS, Kurasaki T, DiSaia PJ, et al. The effect of route of delivery on regression of abnormal cervical cytologic findings in the postpartum period. Am J Obstet Gynecol 1998;178:1116-20.
29. Chung SM, Son GH, Nam EJ, Kim YH, Kim YT, Park YW, et al. Mode of delivery influences the regression of abnormal cervical cytology. Gynecol Obstet Invest 2011;72:234-8.