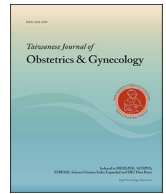




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Original Article

Clinical parameters associated with absence of endocervical/transformation zone component in conventional cervical Papanicolaou smears



Lou Sun ^a, Peng-Hui Wang ^{b, c, d}, Chen-Hui Lee ^e, Tsai-Feng Fu ^f, Min-Min Chou ^a, Sheau-Feng Hwang ^a, Yu-Min Ke ^a, Shih-Tien Hsu ^{a, g}, Chien-Hsing Lu ^{a, c, e, h, i, *}

^a Department of Obstetrics and Gynecology, Taichung Veterans General Hospital, Taichung, Taiwan

^b Department of Obstetrics and Gynecology, Taipei Veterans General Hospital, Taipei, Taiwan

^c Department of Obstetrics and Gynecology, National Yang-Ming University School of Medicine, Taipei, Taiwan

^d Department of Medical Research, China Medical University Hospital, Taichung, Taiwan

^e Department of Pathology and Laboratory Medicine, Taichung Veterans General Hospital, Taichung, Taiwan

^f Graduate Institute of Biomedicine and Biomedical Technology, National Chi Nan University, Nantou County, Taiwan

^g School of Medicine, China Medical University, Taichung, Taiwan

^h Institute of Biomedical Sciences, National Chung-Hsing University, Taichung, Taiwan

ⁱ Rong-Hsing Research Center for Translational Medicine, National Chung-Hsing University, Taichung, Taiwan

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ABSTRACT

Objective: To study clinical factors predicting the absence of endocervical/transformation zone (EC/TZ) components of conventional cervical Papanicolaou (Pap) smears.

Materials and methods: The medical charts of patients who received Pap smears between March 2006 and August 2006 in the hospital were reviewed. The results of their Pap smears were retrieved while their demographic and clinical information were obtained from the medical charts. After excluding 378 cases with incomplete demographic data and 1397 cases with a history of pelvic irradiation, pelvic malignancy, and hysterectomy, 5662 cases were enrolled for data analysis. The relationship between clinical parameters and the absence of EC/TZ component was analyzed by Pearson Chi-square tests with Yates continuity correction and binary logistic regression tests.

Results: The incidence of satisfactory but absence of EC/TZ component was 8.7% (491/5662). Pregnancy increased the absence of EC/TZ component [odds ratio (OR): 2.84, 95% confidence interval (CI): 2.14–3.77, $p < 0.0001$]. Postpartum status and endocervical polyps decreased incidence (OR: 0.61, 95% CI: 0.38–0.98, $p = 0.043$ and OR: 0.33, 95% CI: 0.25–0.44, $p < 0.0001$, respectively).

Conclusions: Pregnancy is the only clinical factor associated with increased incidence of absence of EC/TZ cells. For these pregnant women undergoing a Pap smear, a more effective strategy may be needed to get a satisfactory smear with adequate EC/TZ components.

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Introduction

In the 1988 Bethesda System, specimen adequacy of a Papanicolaou (Pap) smear includes one category called *less than optimal*, which indicates that the smear provides useful diagnostic

information but is less than optimal due to obscurity caused by inflammation, absence of endocervical cells, endocervical mucus, or squamous metaplastic cells [1]. The terminology has since been revised to *satisfactory for evaluation but limited by* in the 1991 Bethesda system [2]. In the 2001 Bethesda system, the terminology is eliminated and replaced by *presence or absence of endocervical or transformation zone [EC/TZ] components or other quality indicators such as partially obscuring blood or inflammation* [3]. From the report of the Cervical Cancer Screening Registration System of the Health Promotion Administration, Ministry of Health and Welfare,

* Corresponding author. Department of Obstetrics and Gynecology, Taichung Veterans General Hospital, 160 Chung-Kang Road Section 3, Taichung City 40705, Taiwan.

E-mail address: chlu@mail.vghtc.gov.tw (C.-H. Lu).

Taiwan, 25.6% of all Pap smears were *less than satisfactory* [4], including 35.9% that were due to the absence of EC/TZ cells. This means that 9.2% of all Pap smears are satisfactory but without EC/TZ cells. Thus, this issue has a significant impact on a large portion of the population who receive Pap smear examinations and to physicians who take the smears.

The absence of EC/TZ components was initially found to decrease the sensitivity of detecting epithelial abnormalities and even cervical cancers [5–8]. Later studies that used better study designs and even larger populations failed to establish an association between the lack of endocervical cells and the increased incidence of high-grade diseases or cervical cancers [9,10]. There are currently no randomized trials or meta-analyses on this issue [11].

For patients with a negative smear and absence of EC/TZ components, the American Society for Colposcopy and Cervical Pathology suggests repeat Pap smear in 12 months. In cases with a history of minor cervical abnormalities or inadequate smear history or procedures, repeat smear within 6 months is beneficial [12]. The impact of the absence of endocervical cells is immense to both patients and doctors. However, the clinical conditions associated with absence of EC/TZ cells have never been studied. Therefore, this retrospective study was designed to explore the clinical conditions associated with absence of EC/TZ cells.

Materials and methods

The materials and methods used here had been published in previous studies [13,14]. The Institutional Review Board of Taichung Veterans General Hospital approved the study. Patients who received conventional Pap smears between March 2006 and August 2006 were enrolled. The results of their Pap smear were retrieved from the Department of Pathology and Laboratory Medicine. Their demographic and clinical information were obtained from their medical charts, as recorded by the attending physicians who took the Pap smears.

In terms of the whole procedure of Pap smear examination, the cervical smears were taken with Ayre's spatulas, endocervical cytobrushes, or a combination with attempts to scrub the whole transformation zone. Findings of pelvic examination were also recorded. The smears were fixed in separate bottles of 95% alcohol for fixation, stained using the Papanicolaou technique, screened by qualified cytotechnologists under light microscopy, and then re-screened by a cytopathologist before the formal reports.

In the study period, 7437 Pap smears were taken. After excluding 378 cases due to incomplete demographic data, 7059 cases were included. Their data on history of pelvic malignancy (excluding microinvasive carcinoma of cervix), systemic chemotherapy, pelvic irradiation, cervical conization (including cold knife cone, loop electro-surgical excision procedure, and needle cone), hysterectomy (total abdominal hysterectomy, total vaginal hysterectomy, laparoscopic-assisted vaginal hysterectomy, modified radical hysterectomy, and radical hysterectomy), pregnancy, within 3 months *postpartum* (>20 gestational weeks), vaginal bleeding or spotting, abnormal vaginal discharge (suggestive of infection or foreign body reaction), intrauterine device, and endocervical polyps were obtained. After further excluding 1397 cases with a history of either pelvic irradiation, systemic chemotherapy, pelvic malignancy, or hysterectomy [13], 5662 cases were enrolled for data analysis.

The relationship between clinical parameters with *satisfactory but absence of EC/TZ component* was analyzed by Pearson Chi-square tests with Yates continuity correction and binary logistic regression tests for significance analysis. Statistical significance was set at $p \leq 0.05$. Data were analyzed using SPSS software (SPSS for Windows, version 12.0; SPSS Inc., Chicago, IL, USA).

Results

Some detailed demographic characteristics and quality and results of the Pap smears of the cohort were published before and the parts relevant to this study summarized [13,14]. The median age of the cohort was 44.5 years (range, 15–93 years). Median gravidity was 2.7 (range, 0–15), and median parity was 1.9 (range, 0–12).

Of the 5662 patients enrolled in final analysis, specimen adequacy was *satisfactory* in 4919 (86.9%), *satisfactory but absence of EC/TZ component* in 491 (8.7%), and *unsatisfactory for evaluation* in 252 (4.5%). The incidence of abnormal Pap smears equals to or greater than atypical cells was 4.53%.

On an attempt to explore the clinical factors by univariate analysis, only pregnancy was associated with increased incidence of *satisfactory but absence of EC/TZ component* (Table 1). Among the 304 pregnant women who received Pap smears in the hospital, 78 (25.6%) had *satisfactory but absence of EC/TZ component*. By contrast, age > 50 years and menopause were associated with lower incidence of *absence of EC/TZ component*.

When these parameters were further analyzed by multivariate binary logistic regression test, pregnancy was found to be significantly associated with more *satisfactory but absence of EC/TZ component* [odds ratio (OR): 2.84, 95% confidence interval (CI): 2.14–3.77, $p < 0.0001$; Table 2]. However, within 3 months *postpartum* and the presence of endocervical polyps were associated with a lower incidence (OR: 0.61, 95% CI: 0.38–0.98, $p = 0.043$; and OR: 0.33, 95% CI: 0.25–0.44, $p < 0.0001$, respectively; Table 2).

Discussion

Given the proportion of *absence of EC/TZ component* in a large population receiving Pap smears, correct management must be re-emphasized [4]. According to the American Society for Colposcopy and Cervical Pathology guidelines [15], women with a routine Pap

Table 1
Predictive factors for *satisfactory but absence of endocervical/transformation component* by univariate analysis.

Variables	Absence (n)	Reference (n)	p
Age			< 0.0001
≥ 50 y	64 (3.8)	1618 (96.2)	
< 50 y	427 (11.5)	3301 (88.5)	
Menopause			< 0.0001
Yes	37 (2.6)	1397 (97.4)	
No	454 (11.4)	3522 (88.6)	
S/p Conization			0.084
Yes	26 (6.5)	371 (93.5)	
No	465 (9.3)	4548 (90.7)	
Pregnancy			< 0.0001
Yes	78 (25.7)	226 (74.3)	
No	413 (8.1)	4693 (91.9)	
Within 3 mo PP			0.254
Yes	19 (7.0)	254 (93.0)	
No	472 (9.2)	4665 (90.8)	
Vaginal bleeding			0.595
Yes	32 (10.1)	286 (89.9)	
No	459 (9.0)	4633 (91.0)	
Abnormal discharge			0.513
Yes	36 (8.1)	408 (91.9)	
No	455 (9.2)	4511 (90.8)	
IUD insertion			0.865
Yes	16 (9.8)	148 (90.2)	
No	75 (9.1)	4771 (90.9)	
Endocervical polyps			0.080
Yes	4 (3.8)	102 (96.2)	
No	487 (9.2)	4817 (90.8)	

PP = *postpartum*; Absence = satisfactory Pap smear but absence of endocervical/transformation zone component; N = number; Reference = satisfactory Pap smear, including clear demonstration of endocervical/transformation zone component.

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