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Is colposcopic evaluation necessary in all women with postcoital bleeding?

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ABSTRACT

Objective: To evaluate what extent postcoital bleeding (PCB) is an indicator of cervical cancer (CIN2 (+)).
Methods: This is a retrospective cohort study. Between 2007 and 2013, amongst all referred patients, a total of 1491 consecutive women who had both conventional cytology and cervical biopsy were enrolled in the study. Of those 237 women have PCB, according to biopsy results, subjects were divided into two groups: CIN1 (−) and CIN2 (+). Multiple logistic regressions was used to construct a model to predict the occurrence of CIN 2 (+) based on age, menopause, marriage status, smoking, PCB, HPV and cytology.
Results: Among the all women with CIN 2 (+) colposcopy guided biopsy result, PCB was 13.1% (53/406). The relationship between biopsy results and age, parity, menopausal status, marital status, smoking, presence of PCB, HPV DNA, and cytology is statistically significant ($p = 0.012$, $p = 0.001$, $p = 0.023$, 0.013, $p > 0.001$, $p = 0.038$, $p < 0.001$, $p < 0.001$, respectively). According to regression analysis only smoking, HPV (+) and abnormal cytology increase the probability of CIN2 (+); 1.687 times ($p = 0.018$), 4.065 times ($p < 0.001$), 5.787 times ($p = 0.001$) respectively. Having PCB only does not indicate an increased risk of CIN2 (+).
Conclusion: Colposcopic examination and biopsy should be performed only in the situation where women have PCB and any of the following: smoking, positive HPV, or abnormal cytology.

Introduction

Postcoital bleeding (PCB) frequently occurs in sexually active women. The estimated prevalence of postcoital bleeding is 6% in menstruating women. Currently, there is no evidence or recommendations from the American College of Obstetricians and Gynecologists (ACOG) or the Royal College of Obstetricians and Gynecologists (RCOG) in the standard of care for postcoital bleeding [1–5]. Whether PCB is in most cases associated with mild cervical pathology requiring no further investigation, and in rare cases, PCB can be the first sign of cervical cancer, is still unknown. There is no evidence from randomize control trials to answer this question [4,5]. Variations in study design and statistical analysis, study locations (developed or undeveloped countries) are the reasons beyond this dilemma [1,6,7]. Furthermore PCB shows multiple etiologies in which most are benign such as cervicitis or cervical polyps.

In the absence of current consensus, we aim to introduce skepticism about the standardize management of PCB and to evaluate whether colposcopy guided biopsy is essential to PCB patients with normal cervix on speculum examination. Secondly, we aim to better identify patients at risk for cervical cancer and thereby enabling rapid referral to a specialized center, and suggest a new predictive model for CIN2 (+) (cervical intraepithelial neoplasm) biopsy results.

Materials and methods

Between January 2007 to December 2013, 1491 women were referred to Baskent University School of Medicine Gynecological Oncology Clinic, who had been diagnosed with at least one of the following: abnormal cytology, HPV+, abnormal biopsy results, or suspicious appearing cervix. All of these women were reexamined upon entering the clinic with conventional cytology, colposcopic examination and cervical biopsy, and enrolled in this study. Of the 1491 patients, 237 had PCB. Each patient was asked to describe the PCB in order to distinguish it from other abnormal uterine bleeding or bleeding during menstrual period. During the speculum examination, normal appearing cervix with PCB was confirmed.

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Pregnant patients, patients with a prior hysterectomy, and patients with an abnormal appearing cervix with a mass lesion, were excluded from the study. Conventional cytology and colposcopy-guided biopsy were performed on all PCB patients. All examinations were performed by one senior gynecologist. Patients with positive colposcopic findings underwent a directed biopsy. Only patients with an unsatisfactory colposcopy, had endocervical sampling. Cytology was undertaken using conventional Pap smears in optimal conditions, mostly in the proliferative phase of the menstrual cycle. In case of excessive bleedings, cervical or vaginal infections, cytology was canceled and performed after treatment of infection and sexual abstinence for two days. HPV DNA (Human Papilloma Virus) test was performed in 65 of 237 women. Real-time polymerase chain reaction (PCR) with a commercial kit (Fluorion, Iontek, Turkey) was used to detect HPV DNA in the samples of cervical smears. Standard colposcopic techniques were used, including application of 3% acetic acid and biopsies were taken from abnormal areas. All specimens obtained by cytology and colposcopy guided biopsies, were evaluated by the same pathologists. Demographic data, past obstetric and gynecologic history, menopausal and smoking status, HPV results, cytology and cervical biopsy results were collected and the data analyzed. According to biopsy results, subjects were divided in to two groups: CIN1 (−) and CIN2 (+). CIN1 (−) includes CIN1 or normal cervical biopsy results, and CIN 2 (+) includes CIN 2, or more severe cervical pathology results.

Statistical method

Multiple logistics regression was used to construct a model to predict the occurrence of CIN 2 (+) (response variable) based on biopsy result, age, menopause, marriage status, smoking, PCB, HPV, cytology (exploratory variables). One of the first steps in building a multiple regression model is to identify the explanatory variables that are significantly related to the response variable. In this study, a *t*-test was used to compare the age between two groups. The χ^2 test was used to evaluate the relationship between two categorical variables in the univariate analysis. Table 2 shows the results of this hypothetical analysis. Often, a less restrictive alpha level is used in the univariate analysis to identify a broad range of exploratory variables that might be associated with the response variable. That is, variables with p values less than 0.25 on univariate analysis are considered for inclusion in the model. To model a regression model is to identify the best combination of exploratory variables to include in the model we used forward variable selection. There was no correlation between explanatory variables. To evaluate statistical hypotheses Type-I error rate was taken as $\alpha = 0.05$. SPSS 22.0 (IBM Corporation and other(s) 1989, 2013) was used for statistical analyses.

Results

There were 1491 women that fulfilled the inclusion criteria and were enrolled in the study. Of those, 237 women described having some degree of PCB. Demographic details for the study population are presented in Table 1. Mean age was 39 (SD ± 9.6) and the majority of the subjects were mothers: premenopausal (86.7%), married (81%), non-smoking (59.1%). The relationship between the cervical biopsy results and the possible risk factors are illustrated in Table 2. Apart from the others, only gravida did not demonstrate a statistically significant relationship between the groups ($p = 0.327$). Age significantly changed between groups ($p = 0.012$). The vast majority of patients are married (81%), and have at least one child (range 0–4). The relationship between groups according to the median parity ($p = 0.001$), and marital status ($p = 0.013$) are significant. Only 13% (198/1491) of the women were postmenopausal and the relationship between biopsy and premenopausal status was significant ($p = 0.023$). Most of the women were non-smokers (59%). A significant relationship was found between the groups according to smoking habits. HPV DNA test was performed in total of 509 subjects and only 65 of 237 women with PCB had the HPV DNA test. The HPV DNA test was positive in 42% (215/509) of all women who had HPV, but only 29% (19/65) of the patients with PCB had a positive HPV test. Cytology was normal in 26% (399/1491) of all patients. Of the 374 patients who had CIN 1 (−) cervical biopsy, only 33% (123) were HPV+. Whereas in 25.7% (384/1491) of the patients with abnormal cytology, pathology results revealed CIN2 (+). Distribution of histological results according to cytological results in PCB patients with normal appearing cervix is shown in Table 4. Out of the total 237 total PCB patients, all had normal appearing cervix, cytology, and

Table 1
Patients' charecteristics and hr-HPV status.

Age	Mean	39.06 ± 9.6
	Range	23–65
Parity	Mean	0.61 ± 0.92
	Range	0–4
Menopauosal status	Premenopausal	1293 (86.7%)
	Postmenauposal	198 (13.3%)
Marital status	Married	1207 (81%)
	Single	284 (19%)
Smoking habitus	Smoker	536 (35.9%)
	Non-smoker	882 (59.1%)
hr-HPV status[a]	hr Hpv positive	215 (42.2%)
	hr Hpv negative	294 (57.7%)

[a] hr-HPV status: one or more high risk HPV types; HPV 16,18, 32, 45 are present.

Table 2
Relationship between the cervical biopsy results and the possible risk factors.

	Cervical biopsy results		p^*
	CIN 1 (−)	CIN 2 (+)	
Gravida	1084 (med:2, min–max: 0–18)	406 (med:1, min–max: 0–11)	0.327
Parity	472 (med:0, min–max: 0–10)	244 (med:1, min–max: 0–11)	0.001
Menapousal status			
Premenopausal	929 (85.6%)	364 (89.7%)	
Postmenopausal	156 (14.4%)	42 (10.3%)	0.023
Total	1085	406	
Marriage status			
Married	894 (82.4%)	313 (77.1%)	
Single	191 (17.6%)	93 (22.9%)	0.013
Total	1085	406	
Smoking			
Smoker	692 (66.7%)	191 (50.1%)	
Non-smoker	346 (33.3%)	190(49.9%)	>0.001
Total	1038	381	
HPV			
−	251(67.1%)	43(31.9%)	
+	123 (32.9%)	92 (68.1%)	>0.001
Total	374	135	
Cytology			
−	377 (34.7%)	22 (5.4%)	
+	708 (65.3%)	384 (94.6%)	>0.001
Total	1085	406	
PCB			
−	901 (83%)	353 (86.9%)	
+	184 (17%)	53 (13.1%)	0.038
Total	1085	406	

[*] p value < 0.005 is considered statistically significant.
CIN 1 (−): cervical biopsy results is CIN 1 or less, CIN 2 (+): cervical biopsy results is CIN 2 or more (CIN2, CIN3, various type of cervical cancer), Cytology (−): normal results, Cytology (+): ASCUS, LSIL, HSIL, ASCH, AGC, SCC