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The Importance of Post Coital Bleeding in Countries with Low Level Cervical Cancer Screening

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ABSTRACT

Background & Objective: This study aimed to examine the extent to which postcoital bleeding (PCB) can be a predictive factor for cervical cancer.

Materials & Methods: In this observational study we selected and evaluated 280 females with PCB referred to Kowsar Hospital of Qazvin, Iran from 2017 to 2019.

Results: Among the 189 patients diagnosed as normal in their Pap smear results, one patient had cancer in her biopsy results. A closer look at the biopsy results of the patients showed 45 patients as normal, 64 patients with cervical infection, 31 patients with polyp cervix, 45 patients with cervical intraepithelial neoplasia 1 (CIN 1), and one patients with squamous cell carcinoma (SCC). Among 63 patients diagnosed with atypical squamous cells of undetermined significance (ASCUS), three showed CIN 2 and CIN 3 in their biopsies. Furthermore, out of 21 patients with low-grade squamous intraepithelial lesion (LSIL), three patients had CIN 2 and CIN 3, one patient had carcinoma, and one had SCC. In addition, all of the patients with high-grade squamous intraepithelial lesion (HGSIL) were diagnosed with CIN 2, CIN 3, and SCC.

Conclusion: Because of the higher rate of cervical cancer in women with PCB and inconsistent screening programs in developing countries, it is essential to carefully consider the symptoms of PCB despite having a normal Pap smear.

Keywords: Biopsy, Cervical cancer, Pap smear, Postcoital bleeding

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Introduction

Postcoital bleeding (PCB) consists of spotting or bleeding after sexual intercourse that is not related to a person's menstrual cycle **(1)**. The prevalence of this problem among females in the fertility age is from one to nine percent (1). The most common causes of PCB are cervical pathology, cervicitis, as well as cervical polyps **(2)**. Cervical cancer, which is the third most common type of cancer in women in developed countries and most common type in developing countries **(3)**, and premalignant cervical lesions are also possible causes of PCB **(1, 3)**. However, PCB cases have been significantly decreased in the developed countries because of the regular screening tests in women. Since the dysplasia, that leads to the cervical cancer, is a slow-growing malignancy, screening tests are essential to decrease the rate of cervical cancer **(4)**. It is important to know that cervical cancer can be prevented by regular Pap smear tests and planned gynecological examinations **(5)**. Therefore, all sexually active women over 21 years old must do Pap smear examinations once in every three years **(5, 6)**. In addition, further examinations including human papilloma virus (HPV) test, colposcopy, and if necessary, biopsy are needed after abnormal screening test results **(6)**.

Colposcopy is a specialized, expensive, and invasive medical procedure for directing the biopsy site, used as second line of screening to identify the cervical intraepithelial neoplasia (CIN). Colposcopy directed biopsy, currently is a gold standard procedure in CIN lesions diagnosis, which helps to evaluate the cases of abnormal Pap smear **(7)**. The accuracy of Colposcopy directed biopsy is very high and can detect up to 70%

of carcinoma in situ (CIS) cases (7). Furthermore, this procedure can help physicians in the diagnosis of premalignant cervical lesions, and can help them to determine treatment strategies (8). Lack of colposcopy procedure in abnormal Pap smear tests in CIN cases can lead to higher stages of cervical cancer (9). However, refusal to perform colposcopy is common, especially in cases with low-grade abnormality in Pap smear, which are not clinically significant. On the other hand the value of colposcopy is not clear in all low grade abnormalities, specifically that colposcopy and biopsy are somewhat invasive procedures (9). Nevertheless, in developed countries, the extensive screening programs significantly decreased the number of women with cervical cancer presenting with PCB (10)(11). The positive predictive value of PCB depends on its prevalence in each country. A systematic review in 2006 reported the prevalence of PCB between 0.7 to 9 percent (3).

Therefore, due the inconsistent cervical cancer screening in Iran and since the Pap smear test did not reduce the incidence of cervical cancer by itself, patient's history and clinical examinations are essential in predicting the cervical cancer. Therefore, due to the lack of knowledge on the importance of regular tests and further procedures in cases of abnormality in developing countries, we examined the extent to which PCB can be a predictive factor for cervical cancer. We hypothesized that PCB can increase the rate chances of cervical cancer and it needs to be screened regularly.

Materials and Methods

In this observational, analytical, and epidemiological study, we carefully selected and evaluated 280 women with PCB complaint referred to Kowsar Hospital of Qazvin, Iran from 2017 to 2019. All subjects were in the age range of 21 to 65 years old and voluntarily agreed to participate in the study. The study was approved by the Research Ethics Committee of IR.QUMS.REC.1398.099. A checklist of required information including such variables as age, history of gynecological cancer in a first-degree relative, marriage time, menarche age, contraception method, and smoking habits was developed. Moreover, pregnant women, women with abnormal uterine bleeding (AUB) and women taking topical or systematic hormone medications were excluded from the study.

At the beginning of the study, we examined all the patients and recorded any abnormal findings in their cervix such as polyp, ectropion, etc. A liquid-based Pap smear was taken from all patients. Then, a professional oncologist with 15 years of experience performed Colposcopy directed biopsy. After the procedures, we classified the results into different groups including normal, cervical intraepithelial neoplasia 1 (CIN 1), CIN 2, CIN 3, CIS, and invasive cancer. The IBM SPSS Statistics for Windows, version 24 (IBM Corp., Armonk, N.Y., USA) was used to analyze the data. We recorded mean and standard deviation for quantitative variables and frequency and frequency percentage for the qualitative variables. Finally, the results of diagnostic tests were compared using chi-square with a significance level of 0.05.

Results

We evaluated 280 patients with PCB with a mean age of 37.9 years (age range: 21-65 years). The mean age of menarche in these patients was 12 years and 15 days with a minimum of 10 years and maximum of 14 years. In addition, the mean duration of marriage was 16 years, ranging from one to 50 years. Our results showed that 61.8% of subjects had a history of vaginal delivery, of whom only 5% (14 patients) were postmenopausal patients. In addition, 5.7% of patients did not have any contraception, and about 10.4% had smoking habits. Also, about 10% of patients (28 patients) had a positive family history of cancer. Table 1 shows mean and standard deviation of characteristics of the patients.

Table 2 shows the relationship between Pap smear and biopsy results. Among the 189 patients diagnosed as normal based on Pap smear results, one patient had cancer in her biopsy results. A closer look at the biopsy results of the patients showed 45 patients as normal, 64 patients with cervical infection, 31 patients with polyp cervix, 45 patients with CIN 1, and one patient with squamous cell carcinoma (SCC). Among 63 patients diagnosed with atypical squamous cells of undetermined significance (ASCUS), three showed CIN 2 and CIN 3 in their biopsies. Furthermore, from 21 patients with low-grade squamous intraepithelial lesion (LSIL), three patients had CIN 2 and CIN 3, one had carcinoma, and one had SCC. All the patients with high-grade squamous intraepithelial lesion (HSIL) were diagnosed with CIN 2, CIN 3, carcinoma, and SCC in colposcopy results. Table 3 shows the diagnostic value of Pop smear versus biopsy procedure.

Table 1. Patient's Characteristics

Characteristics	Mean (range), SD – Frequency (%)
Age	36.90(20-62)±7.41
Gravity	2.21(0-10)±1.33388
Parity	2.23(0-7.00)±1.25

Characteristics	Mean (range), SD – Frequency (%)
Abortion	1.88(1-2)±0.32
Menarche age	12.15(10-14)±0.76
Marriage time	16.45(1±50)±9.23
Delivery type	
vaginal	157(61.8%)
Cesarian Section	90(35.4%)
Nulligravid	7(2.8%)
Menopause	14(5%)
Contraception	
No	16(5.7%)
Tubal Ligation	50(17.9%)
OCP	59(21.1%)
Withdrawal	106(37.9%)
IUD	16(5.7%)
Depo Medroxy Progestrone Acetate	11(3.9%)
Barrier	21(7.5%)
Smoker	29(10.4%)
Family History cancer	28(10%)

Table 2. The relationship of Pap smear and Biopsy results

Crosstab			Biopsy						
		No.	Normal	Cervicitis	Cervical polyp	CIN I	CIN II , III	Carsima insita	SCC
Pop Smear	Normal	135 (48.2%)	44 (32.5%)	35 (25.9%)	22 (16.3%)	33 (24.4%)	0	0	1(0.74%)
	Inflammation	54 (19.3%)	4 (7.4%)	29 (53.7%)	9 (16.7%)	12 (22.2%)	0	0	0
	ASC-US	63 (22.5%)	6 (9.5%)	14 (17.7%)	7 (11.1%)	33 (52.4%)	3 (4.8%)	0	0
	LSIL	21 (7.5%)	0	1 (4.8%)	0	15 (71.4%)	3 (14.3%)	1 (4.8%)	1 (4.8%)
	HSIL	7 (2.5%)	0	0	0	0	4 (57.1%)	2 (28.6%)	1 (28.6%)
	Total	280	55 (19.6%)	79 (28.2%)	38 (13.6%)	93 (33.2%)	10 (3.57%)	3 (1.1%)	3 (1.1%)

Table 3. Diagnostic value of Pap smear versus Biopsy procedure

	Biopsy	
Pop smear	Normal	Abnormal
Normal	188	1
Abnormal	76	15
Fisher's exact test		
P value	<0.0001	
P value summary	****	
One- or two-tailed	Two-tailed	
significant (alpha<0.05)	Yes	

Discussion

In the current study, we evaluated 280 patients with PCB to determine the risk of cervical cancer in them. The majority of patients with PCB had benign lesions in cervical biopsy, with 28.2% cervicitis and 13.6% cervical polyp. These findings are similar to the results reported by Tehranian *et al.* (2009) and Cohen *et al.*

(2019), that demonstrated 31.7% and 33.8% cervicitis and 16.3% and 12.4% cervical polyps, respectively **(12, 13)**. Moreover, Rosenthal *et al.* (2001) and Tehranian *et al.* (2009) did not report any pathology in 50% and 16.3% of their patients with PCB, respectively **(12, 14)**. Similarly, in this study, we did not observe any pathology in 32.5% of patients with PCB. In our study, 33.2% of patient were diagnosed with CIN 1 and about 3.57% with CIN 2 and CIN 3, which is similar to the findings reported by Shalini *et al.* (1998) with 3.6% CIN 2 and CIN3 **(16)**. However, the results of Tehranian *et al.* showed a lower level of CIN 2 (2.4%) compared to this study **(12)**.

Furthermore, our study showed that increasing age is a significant risk factor in women with PCB for cervical cancer. In this regard, the mean age of the patients with CIN 2 or higher lesions in biopsy was 41.5 years compared to the mean age of all patients (36.9 years) and patients with benign pathology (32 years). These findings are similar to those of Shalini *et al.* (1998) and Haminishi *et al.* (2015), in which the mean age for patients with cancer was 41.3 and 42.5 years compared to patients with benign pathology as 32 and 33.5 years, respectively **(16, 17)**. Another recent study showed that increasing age is a risk factor for cervical cancer in women with PCB, and they did not find any cervical cancer in women under 35 years old **(18)**. However, contrasting to our results, in one study, age did not have any effect on the rate of cervical cancer or CIN **(19)**, or increasing the risk of CIN 2 and more advanced lesions **(20)**. However, one study showed that older women were less often diagnosed at an early stage of cervical cancer **(21)**. This might be due to the lack of awareness about cervical cancer among older women. Another possible factor is the lack of examinations in the postmenopausal years among these women **(21)**. Therefore, similar to some previous studies, our results highlighted the importance of obstetrics and gynecology services in all women with PCB at any ages in reducing the mortality rate of cervical cancer.

In this study, out of 280 patients with PCB, 2.2% had cervical cancer or CIS. Other studies reported 0.8% cervical cancer among 123 patients **(12)**, 3.3% cervical cancer among 2377 patients **(22)**, and 3% cervical cancer and 0.3% vaginal cancer among 314 patients with PCB **(14)**. In this study, among the three patients with cervical cancer, one had normal Pap smear test (1%), which shows the importance of further examinations with colposcopy, and if necessary, biopsy in decreasing the mortality rate of cervical cancer in women with PCB **(23)**. In fact, in one study carried out in 2010, 15 out of 19 women (78.9%) with previous negative Pap smear history had CIN and CIS **(24)**. A 3-year retrospective study by Sahu *et al.* (2007) reported that 6.9% of women with PCB had dysplasia on histology report **(25)**. In addition, another retrospective histology review in 166 women with PCB and normal Pap smear showed 3.6% of cervical cancer and 9% CIN **(19)**. Another recent study in 2019 showed that 16% of all women diagnosed with cervical cancer had negative Pap smear results **(18)**. Therefore, there is a considerable variation among the studies on women with PCB and cervical cancer, advanced age and specific abnormal cytology **(10, 12, 14, 24, 19)**, We are still uncertain about when women with PCB should be referred for further examination and where they should be seen. However, due to the inconsistency in the cervical cancer screening programs among women, specifically in developing countries, and because the Pap smear tests alone cannot reduce the incidence of cervical cancer, it is recommended that all patients with PCB be referred for colposcopy, and biopsy test if necessary, despite having a normal pap smear.

All women with PCB need an urgent speculum examination to preclude cervical cancer. Although the most common reason of the PCB is benign changes in the cervix, it is crucial to perform colposcopy and biopsy procedures in women with constant PCB, even in cases when the Pap smear results are normal. Because of the higher rate of cervical cancer in women with PCB and inconsistent screening programs in developing countries, it is necessary to pay attention to the symptoms such as PCB despite having a normal Pap smear. However, since this problem grows slowly over time, it is necessary to find and treat it before it causes serious issues. Therefore, based on the results of our study, we highly recommend contemporaneous colposcopy, and if necessary biopsy, for women with PCB, even if their Pap smear test is negative.

However, despite the limitations of the study, the findings are crucial and can help reducing the mortality rate of cervical cancer in women with PCB. We recommend conducting large multicenter studies in the future to provide further information in optimizing the management of PCB.

Conclusion

Acknowledgments

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Conflict of Interest

Authors declared no conflict of interests.

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