Risk Factors for Abnormal Cervical Cytology in Pregnant Women Attending the High-Risk Obstetrics Clinic at the University Hospital in San Juan, Puerto Rico

Jaffet Seda, MD*; Yaniris Avellanet, MD*; Fernando J. Roca, MD*; Eduardo Hernández, MPH†; Sharee A. Umpierre, MD*; Josefina Romaguera, MD, MPH*

Objective: Approximately 30% of women diagnosed with cervical cancer are in their childbearing years, and 5-8% of pregnant women seeking prenatal care are found to have an abnormal Papanicolaou smear. Prenatal visits are an excellent opportunity for cervical cytology testing and patient education because of close follow-up. The objective of this study is to examine the overall prevalence of cervical dysplasia and associated risk factors in pregnant women aged 15 to 30 years attending the high-risk obstetrics clinics at the University Hospital in San Juan, Puerto Rico between December 2005 and May 2007.

Methods: We performed a systematic review of 237 prenatal charts from patients attending the high-risk obstetrics clinics at the University Hospital in San Juan. The variables studied were age, place of birth, gestational age at first visit, gravidity, age at first coitus, number of sexual partners, tobacco use, Papanicolaou smear results, and cervical gonorrhea and Chlamydia test results. The relationship between cervical cytology results and the aforementioned variables was statistically assessed.

Results: Abnormal cervical cytology was found in 16 (6.8%) of the patients. Of these, 75% were atypical squamous cells of unknown significance (ASCUS), 19% low-grade squamous intraepithelial lesion (LGSIL), and 6% high-grade squamous intraepithelial lesion (HGSIL). Gravidity > 3 was observed in 16.5% of the patients, and 48.7% were in their second trimester of gestation. Their first coitus was at age 17 or earlier (66.5%), and 78% had between 1 and 3 sexual partners. Having a positive Chlamydia test was significantly ($p<0.05$) associated with the risk of having an abnormal cervical cytology. Other variables such as gravidity, age at first coitus, number of sexual partners, and tobacco use were not statistically associated with an abnormal cervical cytology test.

Conclusion: The overall prevalence of cervical dysplasia among pregnant women who attend the high-risk obstetrics clinic at the University Hospital in San Juan, Puerto Rico is similar to what has been reported elsewhere. Among all variables studied, only a positive Chlamydia test was found to be associated with an abnormal cervical cytology test. Given the high number of women seeking prenatal care and the close follow-up provided during this period, prenatal care is an excellent opportunity for cervical cytology testing and patient education. [*P R Health Sci J 2011;1:14-17*]

Key words: Abnormal cervical cytology, Pregnancy, Women in Puerto Rico

Carcinoma of the cervix uteri is the third most common gynecologic cancer in the United States, with an incidence rate of 8.2/100,000 (1). In Puerto Rico, it is 5th most common cancer in women, and its incidence is higher at 10.3/100,000 (2). Previous studies have shown that Hispanic women have a greater propensity for developing invasive cervical cancer (3). This might be related to the fact that they are generally less adherent to screening when compared

*Department of Obstetrics and Gynecology; †Department of Biostatistics and Epidemiology, Graduate School of Public Health, University of Puerto Rico Medical Sciences Campus, San Juan, Puerto Rico

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Address correspondence to: Josefina Romaguera, MD, MPH, Department of Obstetrics and Gynecology, University of Puerto Rico School of Medicine, PO Box 365067 San Juan PR 00936-5067. Tel/Fax: (787) 758-0037, (787) 764-7881 •Email: josefina.romaguera@upr.edu

to white women (4-5). The American College of Obstetricians and Gynecologists, the US Preventive Services Task Force (USPSTF), and the American Cancer Society recommend screening in sexually active women at least every 3 years, starting at age 21 or 3 years after the first coitus (6-8).

Approximately 30% of women diagnosed with cervical cancer are in their childbearing years, and 5-8% of pregnant women seeking prenatal care are found to have an abnormal Papanicolaou smear (9-10). The management of abnormal cytology during pregnancy can be challenging. Further diagnostic studies, such as colposcopy and cervical biopsy, although not contraindicated in pregnancy, are usually deferred until the postpartum period in a patient with atypical squamous cells of unknown significance (ASCUS) or low-grade squamous intraepithelial lesion (LGSIL) (11). High-grade lesions, however, necessitate a colposcopic evaluation and cervical biopsy (11). If invasive cancer is found, treatment will depend on tumor staging, patient's age, gestational age, parity, and her desire to continue the present pregnancy (12).

Given the high number of women seeking prenatal care and the close follow-up provided during this period, prenatal care is an excellent opportunity for cervical cytology testing and patient education. Human papilomavirus (HPV) infection has been recognized as an important and necessary cause in the development of cervical cancer (13). In addition, behavioral, exogenous, or host-related factors have also been implicated in the pathogenesis of cervical cancer.

Women having their first sexual intercourse at age 17 or earlier, as well as an increasing number of sexual partners, increases the risk of developing cervical cancer (14). Increased number of pregnancies, oral contraceptive use, and cigarette smoking have also been associated with cervical cancers, most probably due to hormonal changes (15-16).

Genetics and immune status are host-related cofactors for the development of carcinoma of the cervix. An increased risk has been observed in women with a family history of cervical cancer among first-degree relatives (17). Also, conditions that impair a woman's cellular immune response results in persistent infection and increased risk of developing cervical cancer (13).

Environmental cofactors may also increase the risk of acquisition of HPV and may elicit cervical cancer development. Herpes simplex virus causes a breach in the mucosal integrity and facilitates the entry of HPV into the basal cell layer. In addition, it causes an inflammatory reaction that may suppress the body's cell-mediated immune response (18). By this last mechanism, *Chlamydia trachomatis* has also been associated with HPV infection and its progression to cancer (19).

The purpose of this study was to examine the overall prevalence of cervical dysplasia and associated risk factors in pregnant women aged 15 to 30 years that attended the high-risk obstetrics clinic at the University Hospital in San Juan, Puerto Rico between December 2005 and May 2007.

Methods

Data collection was performed through a systematic review of 237 randomly-selected prenatal charts from patients that attended the high-risk obstetrics clinic at the University Hospital in San Juan, Puerto Rico between December 2005 and May 2007. The variables studied were age, place of birth, gestational age at first visit, gravidity, age at first coitus, number of sexual partners, tobacco use, Papanicolaou smear results, and cervical gonorrhea and Chlamydia test results. In order to assess the relationship between cervical cytology results and the aforementioned variables, bivariate analysis was performed using contingency tables and the chi-square test. Statistical significance was set at $p<0.05$. The database construction and statistical analyses were perfomed using the statistical software STATA version 9 (STATA Corp, College Station, TX, USA).

Results

Two-hundred and thirty-seven randomly selected prenatal charts were evaluated. The majority of patients were born in Puerto Rico (84.1%), followed by the Dominican Republic (8.6%). Their gravidity was ≤ 3 in 83.5%, and 48.7% were in their second trimester of gestation. Their first coitus was before or at age 17 in 66.5%, and 78.0% had between 1 and 3 sexual partners.

The overall prevalence of an abnormal cervical cytology test was 6.8%. Of these,75% ASCUS, 19% LGSIL, and 6% high-grade squamous intraepithelial lesion (HGSIL) (data not shown). The 15-19 and 20-24 age groups were the most affected (37.5% each). Table 1 shows the characteristics of the study sample according to the presence or absence of cervical dysplasia. Among patients with an abnormal cervical cytology test, 18.7% reported having more than 3 pregnancies, 80.0% had their first coitus at age 17 or earlier, 25% had more than 3 lifetime number of sexual partners, and 12.5% were current or past smokers. However, differences between these parameters were not significant when compared to patients with normal cervical cytology results.

Regarding other sexually transmitted infections, 91.1% were negative for *Chlamydia trachomatis*, and 99.2% for *Neisseria gonorroheae*. A positive Chlamydia test was found in 31.2% of the patients with an abnormal cervical cytology as compared to 7.3% with a normal cervical cytology results ($p=0.008$).

Discussion

The overall prevalence of cervical dysplasia among this group of pregnant women attending the high-risk obstetrics clinic at the University Hospital in San Juan, Puerto Rico is similar to what has been reported elsewhere. Having a positive test for chlamydia was statistically associated with the risk of an

abnormal cervical cytology test. Cervical chlamydial infection causes an inflammatory reaction that suppresses the local T-cell immune response, thus facilitating the establishment of an HPV infection. Among sexually transmitted bacterial infections, chlamydia is the most prevalent. In 2007, its incidence in women was 544.8/100,000 (20). In Puerto Rico, the overall incidence was lower at 201/100,000. In 2009, a total of 19,333 chlamydia tests were done in Puerto Rico in women younger than 26 years, with a positivity rate of 9.8% (21).

It is important to detect and promptly treat chlamydial infection in women since it may have serious sequelae, including pelvic inflammatory disease, infertility, ectopic pregnancy, and chronic pelvic pain (22). The Center for Disease Control and Prevention (CDC) recommends screening for chlamydia in all sexually active women <20 years of age; in women 20-24 years of age if one of the following risk factors is present: inconsistent use of barrier contraceptives or a new sexual partner or multiple sexual partners during the previous 3 months; and in women >24 years of age if both risk factors are present (inconsistent use of barrier method plus new or multiple sexual partners). Pregnant women should be screened during the first prenatal visit and in the third trimester if high risk factors are present (22). Despite these strong recommendations, only 40% of young women are screened per year (23). More aggressive screening and patient education programs need to be implemented by community physicians and government authorities.

Our study has some limitations. First, the study was based on medical chart review and due to its retrospective nature, other important sociodemographic or lifestyle information was not available for evaluation. In addition, our results did not show evidence of statistical association between known risk factors for HPV infection (i.e. increasing gravidity, greater number of sexual partners, and tobacco use) with an abnormal Papanicolaou smear. Possible explanations include a type II error due to the small number of patients with an abnormal cervical cytology test, a lack of statistical power, sampling bias, and absent data.

In conclusion, our study has shown that the overall prevalence of cervical dysplasia among pregnant women who attend the high-risk obstetrics clinic at the University Hospital in San Juan, PR is similar to what has been reported elsewhere. Among all variables studied, only a positive Chlamydia test was found to be associated with an abnormal cervical cytology test. Given the high number of women seeking prenatal care and the close follow-up provided during this period, prenatal care is an excellent opportunity for cervical cytology testing and patient education.

Table 1. Characteristics of the study population according to presence and absence of cervical dysplasia

Variable	N	Pap smear negative n (%)	Pap smear positive n (%)	Total	p-value
Age (years)	234				
15-19		60 (27.5)	6 (37.5)	66 (28.2)	
20-24		83 (38.1)	6 (37.5)	89 (38.0)	0.632
25-30		75 (34.4)	4 (25.0)	79 (33.8)	
Place of Birth	232				
Puerto Rico		181 (83.8)	14 (87.5)	195 (84.1)	
United States		16 (7.4)	0 (0.0)	16 (6.9)	
Dominican Republic		18 (8.3)	2 (12.5)	20 (8.6)	0.593
Other		1 (0.5)	0 (0.0)	1 (0.4)	
Gravidity	237				
≤ 3		185 (83.7)	13 (81.3)	198 (83.5)	
> 3		36 (16.3)	3 (18.7)	39 (16.5)	0.732
Trimester	230				
1		72 (33.6)	8 (50.0)	80 (34.8)	
2		107 (50.0)	5 (31.2)	112 (48.7)	0.320
3		35 (16.4)	3 (18.8)	38 (16.5)	
Age at 1st coitus (years)	227				
≤ 17		139 (65.6)	12 (80.0)	151 (66.5)	0.252
> 17		73 (34.4)	3 (20.0)	76 (33.5)	
Number of sex partners	227				
1-3		165 (78.2)	12 (75.0)	177 (78.0)	0.757
≥ 4		46 (21.8)	4 (25.0)	50 (22.0)	
Cigarette smoking	237				
Never		199 (84.0)	14 (87.5)	213 (89.9)	
Ever		22 (9.3)	2 (12.5)	24 (10.1)	
Chlamydia test	236				0.008
Negative		204 (92.7)	11 (68.8)	215 (91.1)	
Positive		16 (7.3)	5 (31.2)	21 (8.9)	
Gonorrhea	237				
Negative		219 (99.1)	16 (100.0)	235 (99.2)	>0.999
Positive		2 (0.9)	0 (0.0)	2 (0.8)	

Resumen

Objetivo: Cerca del 30% de las mujeres con cáncer cervical se encuentran en edad reproductiva, y entre el 5% y 8% de las mujeres embarazadas tienen un resultado anormal en la prueba de citología cervical. Las visitas prenatales son el momento ideal para realizar dicha prueba debido al seguimiento cercano que se brinda a las pacientes. El objetivo de este estudio fue evaluar la prevalencia general de la displasia cervical y los factores de riesgo asociados en mujeres embarazadas de entre 15 y 30 años de edad que asistieron a la clínica de obstetricia de alto riesgo en el Hospital Universitario de San Juan, Puerto Rico entre diciembre de 2005 y mayo de 2007. Métodos: Realizamos una revisión sistemática de 237 récords prenatales de pacientes que asisten a la clínica de obstetricia de alto riesgo en el Hospital Universitario de San Juan. Las variables

estudiadas fueron edad, lugar de nacimiento, edad gestacional al momento de la primera visita, gravidez, edad al momento del primer coito, número de parejas sexuales, uso de tabaco, resultado de prueba citología cervical, y resultado de prueba cervical para clamidia y gonorrea. La relación entre citología cervical y dichas variables fue evaluada estadísticamente. Resultados: Una prueba de citología cervical anormal fue observada en 6.8% de las pacientes. De éstos, 75% fue ASCUS, 19% fue LGSIL y 6% fue GSIL. Gravidez > 3 se observó en 16.5% de las pacientes y 48.7% se encontraba en el segundo trimestre de gestación. La edad al momento del primer coito fue en o antes de los 17 años (66.5%), y 78% tenía entre 1 y 3 parejas sexuales. Una prueba positiva de clamidia se asoció significativamente ($p<0.05$) con la posibilidad de obtener un resultado de citología cervical anormal. Otras variables como gravidez, edad al momento del primer coito, número de parejas sexuales y uso de tabaco no se asociaron significativamente con tener un resultado de citología cervical anormal. Conclusión: La prevalencia general de la displasia cervical entre mujeres embarazadas que asisten a la clínica de obstetricia de alto riesgo en el Hospital Universitario de San Juan, Puerto Rico es similar a la reportada en otros centros hospitalarios. De las variables estudiadas, una prueba positiva para clamidia fue la única asociada a una prueba de citología cervical anormal. Dado el alto número de mujeres que reciben cuidado prenatal y el seguimiento cercano que se les brinda, este período es ideal para educar y realizar la prueba de citología cervical.

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