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CLINICAL ARTICLE

Results of screening for cervical cancer among pregnant and non-pregnant women in Brazil

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ABSTRACT

Objective: To compare cervical cytology test results among pregnant and non-pregnant women, and to assess associations with age, screening history, and onset of sexual intercourse. *Methods:* A retrospective analysis was conducted of cervical smears obtained from women aged 18–34 years in the Campinas region of Brazil between January 2000 and December 2009. Eligible participants had not undergone cytological screening within the previous year and had no history of precursor lesions or cervical cancer. Multinomial logistic regression was performed for different age groups, with high-grade squamous intraepithelial lesions (HSILs) as the endpoint. *Results:* Overall, 3072 (0.4%) of 861 353 non-pregnant women and 135 (0.4%) of 37 568 pregnant women had HSILs. Odds of HSIL among pregnant and non-pregnant women did not differ in any age group. An increased age at first sexual intercourse among pregnant women reduced odds of HSILs in all age groups (odds ratio 0.9 [95% confidence interval 0.8–0.9] for all). Among women aged 21–24 years, 25–29 years, and 30–34 years, some associations were identified between an interval of less than 5 years since previous screening and reduced odds of HSILs. *Conclusion:* Mandatory cervical cytology screening does not seem to be necessary for pregnant women; protocols in place for non-pregnant women should be followed.

1. Introduction

Implementation of screening examinations can reduce the incidence of cervical cancer and its associated mortality, but such reductions are dependent on the age of the patients, the quality of the service, and the coverage of programs [1–3]. Indeed, cervical cancer continues to have a high incidence and is one of the leading causes of death among women as a result of the weakness of screening programs in low-income countries [1,4,5].

The average time for persistent HPV infection to progress to cervical cancer is 12–15 years [5,6]. However, most infections heal spontaneously without inducing a malignant phenotype. Consequently, the development of cancer following HPV infection could be considered a rare complication that reflects viral carcinogenesis as a multifactorial process [5,6].

Many women undergo screening for cervical cancer during pregnancy [7,8]. Women aged 18–35 years have the highest concentration of pregnancies and the highest rates of HPV infection and cervical precursor lesions [9]. Furthermore, it has been suggested that women younger than 30 years should undergo screening exclusively by cytology examination [3,8]. Because cervical carcinoma is frequently diagnosed during pregnancy [8–10], it would be useful to determine whether the prevalence of precursor lesions is similar between pregnant women and their non-pregnant counterparts.

Current opinion suggests that a 3-year interval between cytological examinations is sufficient [3]. Many recommendations indicate that women should receive their first screening examination when aged 20–25 years; however, individual guidelines vary from 18 years to 30 years [2–4,11]. The diagnosis of precursor lesions can lead to diagnostic and therapeutic procedures that cause future obstetric and neonatal morbidity for women younger than 18 years [12]. Additionally, there is a lack of objective information about whether the risk of neoplastic changes in the cervix among pregnant women is the same as among non-pregnant women.

The aim of the present study was to compare the prevalence of various cytology test results among pregnant and non-pregnant women and to evaluate associations with age, time since last cervical smear, and age at first sexual intercourse.

2. Materials and methods

A retrospective analysis was conducted of cervical smears obtained from pregnant and non-pregnant women aged 18–34 years who were

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receiving primary care in the public health system in approximately 70 cities within the Campinas area of Brazil between January 1, 2000, and December 31, 2009. Samples were included in the present study when no other screening examinations had been performed within the previous year and the patient had not been previously diagnosed with precursor lesions or cervical cancer. In addition, only women for whom data for age at screening and age at first sexual intercourse were available were included. Cervical smears that were incorrectly labeled, classified as unsatisfactory, or performed for purposes other than screening were excluded from the analysis.

Approval for the present study was obtained from the institutional review board of the State University of Campinas (No. 375/2010). The institutional review board granted a waiver for the requirement to obtain a signed consent form because the analyses performed in the present study were retrospective in nature and the anonymity of the women was preserved.

All cervical smear tests were analyzed at the Laboratory of Cytopathology at the Women's Hospital of the State University of Campinas, Campinas, Brazil. Cytology test results were categorized as negative for intraepithelial lesions or malignancy, atypical squamous cells of undetermined significance (ASCUS), low-grade squamous intraepithelial lesion (LSIL), or high-grade squamous intraepithelial lesion (HSIL). Cytotechnologists initially analyzed the cervical smears; pathologists reviewed any suspicious or positive test results, as well as 30% of all negative test results, in accordance with internal quality control. The results were reported using the Bethesda system [13,14].

During the gynecologic examination, data for characteristics, age at screening, age at first sexual intercourse, and time since last screening examination were recorded on a specific form. Cytology test results were added to the patient form by the laboratory staff. All data were entered into the information system of the Laboratory of Cytopathology, which had been constructed for screening management and quality assessment purposes.

Both pregnant and non-pregnant women were stratified by age group (<21 years, 21–24 years, 25–29 years, and 30–34 years). To analyze the relationship with the cytology test result, age at first sexual intercourse was considered to be a continuous numerical variable. The interval between the current screening examination and the last screening examination was categorized as first examination, 1 year, 2 years, 3 years, 4 years, and at least 5 years.

Data were analyzed using SAS version 2.9 (SAS Institute, Cary, NC, USA). Descriptive data are presented as absolute (number) and relative (percentage) values. Multinomial logistic regression analysis was performed for every age group, taking HSIL as the endpoint. The independent variables were pregnancy, age at first sexual intercourse, and interval since the last screening examination. The odds ratio (OR) and 95% confidence interval (CI) were calculated for the logistic regression analyses. An OR greater than 1.0 was considered a risk factor, whereas an OR less than 1.0 was considered a protective factor. $P < 0.05$ was considered statistically significant.

3. Results

From the pool of 2 505 154 potential participants, 898 921 met the inclusion criteria. Among eligible patients, 37 568 (4.2%) were pregnant and 861 353 (95.8%) were not pregnant. The mean age was 26 years (range 18–34) and age at first sexual intercourse was 13–26 years. Overall, 877 796 (97.6%) included patients had negative cytology results, 10 895 (1.2%) had ASCUS, 7023 (0.8%) had LSILs, and 3207 (0.4%) had HSILs. Data for screening history showed that 114 163 (12.7%) women had undergone their first screening examination, 443 168 (49.3%) had undergone their previous screening examination 1 year before, and 30 563 (3.4%) had undergone their previous screening examination at least 5 years before.

The distribution of the cytology test results is presented in Table 1. The frequency of HSIL was the same among pregnant and non-pregnant women overall (0.4%), but varied by age group. The prevalences of ASCUS and LSIL decreased with increasing age among both pregnant and non-pregnant women, whereas negative cytology test results showed a slight increase with increasing age.

In multinomial logistic regression analysis, no statistically significant differences for the prevalence of HSIL were detected between pregnant and non-pregnant women in any age group (Table 2). Furthermore, irrespective of age at current screening, age at first sexual intercourse was a protective factor for HSIL: the older the individual at first sexual intercourse, the lower the chance of a cytology test result of HSIL (Table 2).

Regarding the time since the last screening examination, no association was found between the examination interval and the prevalence of HSIL among women younger than 21 years (Table 2). For women aged 21–24 years, intervals between cytology examinations of 1, 2, or 3 years were protective for HSIL versus an interval of at least 5 years (Table 2). Among women aged 25–29 years, women who had undergone their first examination were more likely to have a result of HSIL than were women whose underwent screening at least 5 years ago, whereas those who underwent screening 1 year and 2 years were less likely (Table 2). Among women aged 30–34 years, women who had undergone screening 1, 2, 3, or 4 years previously were less likely to be diagnosed with HSIL than were those who underwent screening 5 years previously (Table 2).

4. Discussion

The present study found no difference in the prevalence of HSIL between pregnant and non-pregnant women, irrespective of age at current screening, time since the previous screening examination, and the age at first sexual intercourse. In this context, it should be noted that the accuracy of the cytology examination does not vary with gestation [10]. Moreover, our results are in concordance with current literature [9,15] because rates of HSIL do not differ between pregnant and non-pregnant women, even when stratified by risk factors (age, time interval between examinations, and age at first sexual intercourse). By contrast, rates of HPV infection are similar between these two groups of women [8,9].

Pregnancy and childbirth have been suggested to influence the natural history of cervical cancer [9,10,15,16] and the prevalence of HPV infection [17], which suggests that pregnancy is not a risk factor for an abnormal cytology test result. In addition, Lee et al. [9] found no difference in overall survival between pregnant and non-pregnant women with early stage carcinoma of the cervix.

The findings of the present study question the recommendation that all pregnant women should undergo a routine cytology examination as part of their prenatal care [7,8]. The American College of Obstetricians

Table 1
Cytology test results for pregnant and non-pregnant women stratified by age.[a]

Age, y	Total	Cytology test result			
		Negative[b]	ASCUS	LSIL	HSIL
Non-pregnant women					
<21	136 598	132 062 (96.7)	2129 (1.6)	1922 (1.4)	485 (0.4)
21–24	212 312	206 483 (97.3)	2960 (1.4)	2045 (1.0)	824(0.4)
25–29	261 363	255 690 (97.8)	2992 (1.1)	1709 (0.7)	972 (0.4)
30–34	251 080	246 829 (98.3)	2409 (1.0)	1051 (0.4)	791 (0.3)
Total	861 353	841 064 (97.6)	10 490 (1.2)	6727 (0.8)	3072 (0.4)
Pregnant women					
<21	10 066	9792 (97.3)	129 (1.3)	112 (1.1)	33 (0.3)
21–24	11 428	11 148 (97.5)	141 (1.2)	103 (0.9)	36 (0.3)
25–29	9990	9798 (98.1)	90 (0.9)	57 (0.6)	45 (0.5)
30–34	6084	5994 (98.5)	45 (0.7)	24 (0.4)	21 (0.3)
Total	37 568	36 732 (97.8)	405 (1.0)	296 (0.8)	135 (0.4)

Abbreviations: ASCUS, atypical squamous cells of undetermined significance; LSIL, low-grade squamous intraepithelial lesion; HSIL, high-grade squamous intraepithelial lesion.
[a] Values given as number or number (percentage).
[b] Negative for intraepithelial lesion or malignancy.