Original
articleEffect of concurrent lower genital tract infections
on cervical cancer screening

J R Schwebke, M E Zajackowski

Background and objectives: Although women attending STD clinics are at high risk for cervical cancer, most STD programmes do not include Papanicolaou (Pap) smears in their routine screening procedures. Concerns regarding reliability of this test in a population with a high rate of active infection are often raised. The objective of this study was to analyse the associations between STD diagnosis/clinical syndromes and unsatisfactory and abnormal Pap smears.

Methods: Retrospective analysis of Pap results and medical records from women attending an inner city STD programme.

Results: Of the 1202 patients analysed, 3.2% had squamous intraepithelial lesions (SIL) and 3.5% had smears which were unsatisfactory because of the thickness of the specimen. There were no associations between STD diagnoses and SIL; however, the presence of cervical inflammation was significantly associated with SIL. Pap smears which were unsatisfactory because they were too thick were also associated with the clinical finding of cervical inflammation.

Conclusions: The presence of active infection did not preclude the detection of SIL on Pap smears. The percentage of unsatisfactory smears resulting from inflammation was low.

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Keywords: cervical cancer; genital tract; infection

Introduction

Cancer of the cervix remains an important health problem in the USA, accounting for 15 000 new cases of cancer annually.¹ Tragically, many of these cases could have been prevented by early detection of precursor lesions with the use of Papanicolaou (Pap) smear screening.^{2,3}

Women attending sexually transmitted diseases (STD) clinics are at particular risk for cervical cancer. Inner city STD clinics, in particular, have traditionally served patients who lack access to other healthcare resources, including minorities and adolescents. Rates of human papilloma virus (HPV) infection, which appears to be necessary for the development of cervical cancer, are high in this group.^{4,5} Cancer of the cervix is epidemiologically linked with increasing numbers of sexual partners and age at first intercourse.⁶ Despite serving this high risk population, most STD clinics do not include Pap smears as part of their routine services. Reasons for this omission include lack of resources and a belief among practitioners that Pap smears obtained from women with an active lower genital tract infection are difficult to interpret and perhaps unreliable, despite the lack of data to support the latter. Proponents of cervical cancer screening in the STD clinic setting acknowledge these real and perceived difficulties, yet point out that the STD clinic may be the sole healthcare provider for that patient.

In 1991, the Chicago Department of Health (CDOH) STD clinics began a pilot programme for cervical cancer screening to determine the effectiveness and feasibility of this service in an STD clinic population with high rates of lower genital tract infections. The objective of this study was to analyse the relations between clinical findings, STD diag-

noses, and cervical cytology. Of particular interest were questions concerning the relations between clinical findings and/or STD diagnoses and the ability of the cytologist to detect the presence of squamous intraepithelial lesions (SIL), and the quality of the Pap smear specimen.

Methods

The analysis is a retrospective review of data collected during the first 11 months of the Pap smear screening programme at the CDOH STD clinics. The programme was initiated at the main STD clinic and subsequently extended to two satellite clinics. Clinicians, the majority of whom were physicians, were trained in the technique by the medical director of the clinic. Clinicians were strongly encouraged to perform a Pap smear during the usual STD examination if the patient stated she had not had a Pap smear within the previous 6 months, and if the patient was not menstruating. Clinicians were instructed to perform a Pap smear regardless of the presence of discharge or other signs of infection. Pap smear results were reviewed by the medical director and retraining provided to clinicians with higher than average numbers of patients with unsatisfactory smears. Clinicians were continually encouraged to perform Pap smears on their patients.

CLINICAL PROCEDURES

The clinical examination consisted of inspection of the external genitalia followed by visualisation of the vagina and cervix with a non-lubricated speculum. Vaginal swabs were obtained for vaginal pH, "whiff" test, and wet mount microscopy. Next, the ectocervix was wiped clean with large cotton swabs. Endo-

Chicago Department
of Health, Chicago,
USA

J R Schwebke
M E Zajackowski

Correspondence to:
J R Schwebke, University of
Alabama at Birmingham,
1900 University Boulevard,
229 Tinsley Harrison Tower,
Birmingham, AL
35294-0006, USA.

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cervical specimens were obtained using a cotton swab for Gram stain and gonorrhoea culture. Resources did not permit routine screening for *Chlamydia trachomatis*; however, some screening using an ELISA technique was performed. Lastly, specimens for cervical cytology were obtained from the ectocervix with a wooden spatula rotated 360° and from the endocervix with a cytobrush. Slides were fixed immediately with spray fixative. Serological screening for syphilis was routinely performed.

MICROBIOLOGICAL PROCEDURES

Vaginal candidiasis and trichomoniasis were diagnosed by wet mount microscopy. The diagnosis of bacterial vaginosis was arrived at by use of the Amsel criteria.⁷ The diagnosis of gonorrhoea was made by culture on Thayer-Martin agar media which was processed in a standard fashion using presumptive identification criteria.⁸ Cervicitis was diagnosed clinically by the presence of mucopurulent endocervical discharge and/or additional signs of cervical inflammation such as easily induced endocervical bleeding and oedema.⁹ An active case of syphilis was diagnosed by either a positive darkfield examination and/or a newly reactive syphilis serology or a fourfold rise in titre for patients with a history of prior syphilis. Genital herpes simplex (HSV) and genital warts were diagnosed clinically.

CERVICAL CYTOLOGY

Smears were performed at the Illinois Department of Public Health Laboratory and were interpreted using the Bethesda criteria.¹⁰ Smears interpreted as suboptimal were considered to be unsatisfactory.

FOLLOW UP OF PATIENTS WITH ABNORMAL RESULTS

Patients were informed that they would be contacted by letter in the event of an abnormal result and were asked to provide a reliable mailing address. This was done independently of the initial patient registration process for the clinic. Patients with abnormal results were sent informational letters whose content varied depending on the test results. Patients with unsatisfactory smears were so informed and invited to return to the clinic for a repeat smear if they had no other source of health care. Patients with atypical smears were sent similar letters but advised to wait 3 months before returning for a repeat smear. Patients with SIL were advised of the need for gynaecological follow up and sent a list of low cost providers in the community along with a copy of their test results. All letters included the name and telephone number of the STD clinic medical director and patients were encouraged to call with any questions. Letters were sent via usual mail services. In the event that a letter to a woman with SIL was returned undelivered, further attempts at notification were initiated including field visits if necessary. Resources did not allow for notification of women whose smears showed reactive changes as the sole abnormality.

SURVEY OF STD PROGRAMMES

In order to assess the availability of Pap smears in STD clinics nationwide, questionnaires were mailed to the STD program managers at the 56 other major STD programme project areas within the USA.

DATA ANALYSIS

Historical data were extracted from the patient's computerised STD medical record. Statistical comparisons were made using EPI INFO 6 software program.¹¹ Fisher's exact test or the χ^2 test was used to compare categorical variables and Wilcoxon's test was used to compare continuous variables.

Results

Pap smears obtained between November 1991 and October 1992 were used for the analysis. Pap smears were obtained from 1270 patients which represented approximately 30% of all women seen. Of these, 21 patients had a prior hysterectomy and were eliminated from further analysis. Medical records could not be located for 27 patients and 20 patients presented for repeat Pap smears during the study period (only their initial result was included in the data set). Thus, 1202 individual patients were included in the final analysis.

The age range of the study population was 13 to 74 years with a mean age of 27.8 years and a median age of 26 years. African-Americans represented 98% of the population. Fifty eight per cent of the women had come to the clinic because of symptoms, 29% for a check up, and 13% were contacts of a known case of STD. Thirty per cent of the women admitted to a prior infection with gonorrhoea, 6% had previously been infected with syphilis, and 7% admitted to a previous chlamydia infection. The majority (65%) of smears were from women visiting the main STD clinic.

At the time of their visit, 57% of the women were found to have a vaginal discharge, 11% endocervical discharge, and 14% other signs of cervical inflammation. The prevalence of STD diagnoses was as follows: cervicitis (27%), trichomoniasis (19%), gonorrhoea (13%), bacterial vaginitis (BV) (12%), candidiasis (9%), syphilis (8%), genital warts (2%), genital herpes (1%), and other (34%). The last category included patients prophylactically treated because of exposure to an infected partner, no STD diagnosis, and other miscellaneous STDs.

Of the 1202 women analysed, 38 (3.2%) had SIL; of these, nine (0.7%) had high grade lesions, including two women with carcinoma in situ. Smears were interpreted as normal for 193 women (16%) and as atypical for 94 (7.8%). A total of 811 (67.5%) were labelled as reactive; however, this was the sole interpretation for 714 (59.4%). Of the 97 reactive smears which had an additional diagnosis, 76 (78.3%) were atypical, 15 (15.5%) had low grade SIL, four (4.1%) had high grade SIL, and two (2.0%) were normal. Thus, 19/38 (50%) of the smears with SIL also showed inflammatory changes. Pap smears were

Comparison of women with and without squamous intraepithelial lesions (SIL)

	No SIL (%) (n = 1001)*	SIL (%) (n = 38)	p Value
Median age (years)	27.0	26.0	NS
Race:			
Black	982/1001 (98.1)	38/38 (100)	NS
White	13/1001 (1.3)	0/38 (0)	
Hispanic	6/1001 (0.6)	0/38 (0)	
History of STDs:			
Syphilis	65/1001 (6.5)	1/38 (2.6)	NS
Gonorrhoea	310/1001 (31.0)	8/38 (21.0)	NS
Clinical examination†:			
Vaginal discharge	563/941 (59.8)	23/38 (60.5)	NS
Cervical discharge	103/950 (10.8)	3/37 (8.1)	NS
Cervical inflammation	137/951 (14.4)	10/37 (27.0)	0.04

*Excludes unsatisfactory smears.
†Some clinical examination findings missing.

labelled as unsatisfactory for 163/1202 (13.6%) of patients. Of these, 109 (66.9%) had no endocervical cells, 42 (25.8%) were too thick, and 45 (27.6%) were rejected for other miscellaneous issues such as improper identification or broken slides.

A comparison of women with and without SIL is shown in the table. Unsatisfactory smears were eliminated for the purpose of this analysis. There were no significant differences in mean age, race, or history of STDs between these two groups. The youngest patient with SIL was 15 years while the oldest was 56 years. There were no significant differences between the two groups with respect to clinical findings during the pelvic examination with the exception of the presence of cervical inflammation. Cervical inflammation was noted in 10/37 (27%) patients with SIL as against 137/951 (14.4%) patients without SIL for whom this clinical information was available ($p = 0.04$). There were no statistically significant associations between specific STDs present at the time the Pap smear was obtained and the presence or absence of SIL. All women with SIL were successfully notified by telephone, letter, or field visit with the exception of one patient who could not be located despite numerous attempts.

Some statistically significant relations were observed between specific STD diagnoses and the results of cervical cytology other than SIL. A diagnosis of trichomoniasis was significantly associated with reactive Pap smears as was a clinical diagnosis of genital warts. Among women with reactive smears, 183/811 (22.6%) had trichomoniasis versus 16/228 (7.0%) of those with satisfactory smears without inflammatory changes ($p < 0.001$). For genital warts, 20/811 (2.5%) women with reactive smears had this clinical diagnosis but none of the 228 women without reactive Paps. The presence of BV was negatively associated with cervical atypia. Among women with atypical Paps, 4/94 (4.2%) had BV versus 112/908 (12.3%) women without atypical smears ($p = 0.03$). Unsatisfactory Pap smears as a whole were not associated with any specific STD diagnosis or with any specific clinical abnormality. However, smears labelled as unsatisfactory because they were deemed too thick for interpretation were significantly associated with cervical inflammation. Of 42 women with thick smears, 12 (28.6%) had findings of cer-

vical inflammation versus 157/1102 (14.2%) of those without thick smears ($p = 0.02$). Although not statistically significant, of the 42 women with thick smears, 17 (40.5%) had a clinical diagnosis of cervicitis versus 312/1160 (26.9%) women with cervicitis and a satisfactory smear.

Thirty four STD programme areas responded to the survey. Of these, 19/34 (56%) stated that Pap smears were unavailable at their clinics. At two of the programmes, smears were available at some but not all of the clinics. Of the 13 programmes where Paps were performed, six estimated that $> 60\%$ of women were screened, five estimated 10–30%, and the remaining two estimated $< 10\%$.

Discussion

Cervical cancer screening has been shown to be an effective means of preventing deaths; however, access to screening is not universal. Death rates due to cervical cancer are nearly three times higher in African-Americans than in whites in the USA, suggesting either lack of or delayed access to screening.^{12 13} Cervical cancer screening is less available in low income communities.¹⁴ In a study of women newly diagnosed with invasive cervical cancer in New York, 73% had received recent ambulatory care which had failed to include a Pap smear.¹⁴

There is general agreement that women attending STD clinics represent a high risk population for cancer of the cervix and should ideally be offered screening.^{15–17} Despite this consensus, as evidenced by our survey, and that of others, few clinics actually offer this service, citing difficulty with funding as well as concerns about the reliability of the Pap smear in the setting of acute lower genital tract infection and follow up of patients.^{17 18} Clinics which do offer Pap smears will often defer obtaining a smear if signs of infection are present, an approach suggested in part by the Centers for Disease Control and Prevention.¹⁶ The difficulty with this approach is that the patient may fail to return for a second examination, thus resulting in a “missed opportunity”. Finally, many women have a poor understanding of cervical cancer screening and assume that a Pap smear is being routinely obtained during any pelvic examination.¹⁹

Interestingly, there are few data, if any, to support the assumption that Pap smears are indeed unreliable in the setting of concomitant infection. In a study by Lawley *et al*, 9/78 (11.5%) patients with moderate to severe inflammation noted on Pap smears with an overall interpretation of normal, were found to have dysplasia by colposcopy suggesting that precancerous changes might be obscured by inflammation.²⁰ However, no control group was included in this study to determine the yield of colposcopy among women with normal Paps and little or no inflammation. In our study, there were no positive or negative associations between SIL and STD diagnoses; therefore, it does not appear that the presence of certain STDs leads to false positive Pap smear results. A similar lack of association

between abnormal cytological results and active infection, with the exception of genital warts, was noted by the British Cooperative Group in their study of STD clinic patients.²¹ The small number of women with a clinical diagnosis of genital warts plus lack of specific diagnostic testing for HPV precludes any meaningful analysis of HPV as a risk factor for SIL in our study. Although there still exists the possibility that dense inflammation may obscure the finding of SIL (false negative smears), among the 38 smears with SIL in our study, 19 (50%) were also interpreted as reactive. Thus, the cytopathologist was able to detect important changes despite the presence of inflammation in these women. We also documented an association between SIL and the presence of cervical inflammation as noted on physical examination. These findings are in agreement with those of Eckert *et al* who found a greater percentage of SIL among patients with inflammatory smears than in those without inflammation.²² Koutsky *et al* also found SIL to be associated with past or present cervical infections.²³ Such an association could suggest that the inflammatory disruption of cervical cells promoted detection of the dysplastic process or perhaps served as a promoter of HPV expression. Prospective longitudinal studies are needed to answer these questions.

The overall incidence of unsatisfactory smears during the study period was relatively high (13.6%); however, among these unsatisfactory smears only 42 (3.5%) of all smears taken were judged by the cytologist to be too thick to be satisfactorily interpreted. There were no statistically significant associations between unsatisfactory smears and STD diagnoses, although 40% of women with smears too thick for interpretation had a clinical diagnosis of cervicitis.

The issue of follow up of abnormal results continues to be somewhat problematic. Resources did not permit an extensive search for women with unsatisfactory or atypical smears who were not able to be located by letter. However, of the patients with SIL all were found with the exception of one. Efforts are under way to develop tighter referral linkages with gynaecologists in the private setting to ensure feedback as to the outcome of colposcopy and biopsy.

It is important to note that despite the fact that clinicians were encouraged to incorporate Pap smear screening into their routine, only 30% of all women attending the clinic were sampled during this initial phase of the programme. It is possible, therefore, that selection bias may have occurred. However, the prevalence of specific infections among the women in the study cohort as well as their demographic profile were typical for those of the clinic population as a whole, suggesting that this was a representative sample.

In summary, the prevalence of SIL among women attending the CDOH STD clinics was 3.2%. The detection and occurrence of SIL did not appear to be negatively affected by the presence of infection. Only 3.5% of women screened had Pap smears too thick for interpretation. STD clinics should make every effort to incorporate this important diagnostic test into their routine screening efforts.

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