Cervical cancer screening among HIV-positive women

Retrospective cohort study from a tertiary care HIV clinic

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ABSTRACT

OBJECTIVE To determine the rate of cervical screening among HIV-positive women who received care at a tertiary care clinic, and to determine whether screening rates were influenced by having a primary care provider.

DESIGN Retrospective chart review.

SETTING Tertiary care outpatient clinic in Ottawa, Ont.

PARTICIPANTS Women who were HIV-positive receiving care at the Ottawa Hospital General Campus Immunodeficiency Clinic between July 1, 2002, and June 30, 2005.

MAIN OUTCOME MEASURES Whether patients had primary care providers and whether they received cervical screening. We recorded information on patient demographics, HIV status, primary care providers, and cervical screening, including date, results, and type of health care provider ordering the screening.

RESULTS Fifty-eight percent (126 of 218) of the women had at least 1 cervical screening test during the 3-year period. Thirty-three percent (42 of 126) of the women who underwent cervical screening had at least 1 abnormal test result. The proportion of women who did not have any cervical tests performed was higher among women who did not have primary care providers (8 of 12 [67%] vs 84 of 206 [41%]; relative risk 1.6, 95% confidence interval 1.06 to 2.52, $P<.05$), although this group was small.

CONCLUSION Despite the high proportion of abnormal cervical screening test results among HIV-positive women, screening rates remained low. Our results support our hypothesis that those women who do not have primary care providers are less likely to undergo cervical screening.

EDITOR'S KEY POINTS

- Women who are HIV-positive have an increased risk of developing cervical cancer and require regular cervical screening. Women who receive tertiary HIV care but who do not have primary care providers might be less likely to receive cervical cancer screening. This study sought to determine if having primary care providers increased the likelihood that HIV-positive women received cervical screening.
- The 3-year cervical screening rate for HIV-positive women in this study (58%) was lower than other reports in the literature. The proportion of women who did not have any cervical tests performed was higher among women who did not have primary care providers, but numbers were small in this group.
- The authors found that 33% of HIV-positive women had at least 1 abnormal test result during the study period, whereas the rate of abnormal results among all women in Ontario in 2003 was 4.5%. The authors found a significant relationship between having a low recent CD4 cell count (< 200 cells/μL) and having 1 or more abnormal test results ($P=.04$).

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Dépistage du cancer du col chez les femmes VIH positives

Étude de cohorte rétrospective à partir d'une clinique de soins tertiaires du VIH.

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RÉSUMÉ

OBJECTIF Établir le taux de dépistage cervical chez les femmes VIH positives traitées dans une clinique de soins tertiaire et déterminer si le fait d'être suivies par un intervenant de première ligne influençait le taux de dépistage.

TYPE D'ÉTUDE Étude rétrospective sur dossiers.

CONTEXTE Clinique de soins tertiaires pour patientes externes à Ottawa, Ontario.

PARTICIPANTS Patientes VIH positives suivies à la Clinique d'immunodéficience du campus de l'Hôpital général d'Ottawa entre le premier juillet 2002 et le 30 juin 2005.

PRINCIPAUX PARAMÈTRES À L'ÉTUDE À savoir si la patiente était suivie par un intervenant de première ligne et si elle avait eu un dépistage cervical. On a noté les caractéristiques démographiques des patientes, leur statut HIV, leurs intervenants de première ligne et le dépistage cervical, incluant la date, les résultats et le type d'intervenant ayant prescrit le dépistage.

RÉSULTATS Cinquante-cinq pour-cent des femmes (126 sur 218) avaient eu au moins un dépistage cervical au cours des 3 ans. Trente-trois pour-cent de celles qui avaient eu un dépistage (42 sur 126) avaient au moins un résultat d'examen anormal. La proportion de femmes qui n'avaient eu aucun examen cervical était plus élevée parmi celles qui n'avaient pas d'intervenant de première ligne (8 sur 12 [67%] vs 84 sur 206 [41%]; risque relatif 1.6, intervalle de confiance à 95% 1.06-2.52, P<,05); ce groupe comptait toutefois peu de sujets.

CONCLUSION Malgré la proportion élevée de résultats anormaux au dépistage cervical chez les femmes VIH positives, le taux de dépistage demeurait bas. Ces résultats concordent avec notre hypothèse à l'effet que les femmes qui ne sont pas suivies par un intervenant de première ligne sont moins susceptibles d'avoir un dépistage cervical.

POINTS DE REPÈRE DU RÉDACTEUR

- Les femmes VIH positives risquent davantage de développer un cancer du col et nécessitent un dépistage cervical régulier. Celles qui reçoivent des soins tertiaires pour le VIH mais qui n'ont pas d'intervenant pour des soins primaires sont moins susceptibles d'avoir un dépistage cervical. Cette étude voulait déterminer si le fait d'être suivie par un intervenant de première ligne augmentait la probabilité qu'une femme VIH positive ait un dépistage cervical.
- Dans cette étude, le taux de dépistage cervical aux 3 ans était plus bas (58%) chez les femmes VIH positives que ce que rapportent d'autres études. La proportion des femmes HIV positives qui n'avaient eu aucun examen du col était plus élevée chez celles qui n'avaient pas d'intervenant de première ligne; ce groupe comptait toutefois peu de sujets.
- Les auteurs ont observé que 33% des femmes HIV positives ont eu au moins un résultat d'examen anormal au cours de l'étude, alors le taux pour l'ensemble des femmes de l'Ontario en 2003 était de 4,5%. Ils ont aussi trouvé une relation significative entre le fait d'avoir eu récemment une numération basse des cellules CD4 (<200 cellules/µL) et le fait d'avoir au moins un résultat d'examen anormal (*P*= ,04).

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In Canada, 17.3% (11 191 cases) of the 67 442 positive HIV test results reported since November 1, 1985, and a growing proportion of new HIV diagnoses (26.2% in 2008 compared with 11.7% before 1999) are among women.[1] Transmission of HIV in women is primarily by heterosexual contact (62.3%),[1] and 17.7% of HIV infections occur among those born in countries where HIV is endemic.[1]

Women who are HIV-positive are at increased risk of human papillomavirus infection, cervical cancer, and precancerous lesions compared with uninfected women.[2-7] Current guidelines recommend that HIV-positive women receive Papanicolaou (Pap) tests at their baseline evaluations, again at 6 months, and yearly thereafter for those with normal results.[8-10] Despite these recommendations aimed at addressing their higher risk, cervical screening in HIV-positive women is poor.[11-13]

Having a usual source of medical care increases the frequency of Pap testing among women,[14] as does receiving gynecologic care at the same site as primary care for HIV-positive women.[13] Care of patients with chronic diseases is increasingly focusing on collaborative, interdisciplinary models of care; thus, we sought to further evaluate the added value for preventive services of having a primary care provider.[15,16]

We conducted a retrospective chart review of HIV-positive women followed at a tertiary care clinic to determine the rate of cervical screening and whether this was lower among women who did not have primary care providers.

METHODS

This is a retrospective cohort study of all HIV-positive women who received care at the Ottawa Hospital General Campus Immunodeficiency Clinic between July 1, 2002, and June 30, 2005. This clinic is representative of multidisciplinary immunodeficiency clinics in developed countries and has a variety of patients with a range of demographic characteristics. Of the more than 1200 patients followed at the clinic, more than 20% are women, with approximately half of these being women from countries where HIV is endemic.[17] The province of Ontario provides universal health care (the Ontario Health Insurance Program [OHIP]) to its residents, landed immigrants, and refugees.

Recent evidence indicates that there is a high rate of abnormal vaginal Pap smear results among HIV-positive women after hysterectomy,[18] but the guidelines on this are not clear; thus, we excluded this group to avoid underestimating the rate of Pap smears among the women in our study.

The Ottawa Hospital Research Ethics Board approved this study. Data were collected only until June 2005, as collaborations to improve primary health care for HIV-positive women began after this date.

Data collection

We collected relevant information from patients' medical records, including demographic characteristics, clinic intake, most recent CD4 cell counts and viral load measurements, transmission risk group, and number of clinic visits during the study period. We identified patients with primary care providers by recording the names of providers listed in the medical records and verifying the specialties of the listed providers using the Canadian Medical Directory or the College of Physicians and Surgeons of Ontario database.

Information on cervical screening tests was available from 2 sources, which allowed us to determine the number of tests performed during the study period, cytology results, and performing providers' names. The Ottawa Hospital electronic medical records contain reports of all laboratory tests performed at Ottawa Hospital sites. CytoBase is a medical database managed by the INSCYTE Corporation (**www.inscyte.org/login.jsp**), which captures more than 95% of cervical cytology reports evaluated in community laboratories in Ontario. We reported rates of cervical screening over 3 years in order to be consistent with data reported by the Ontario Cervical Screening Program.[19] Pap test results are reported according to the Bethesda System.[20,21] We classified cervical screening tests performed by family physicians or nurse practitioners as being performed by primary care providers.

Quality control

We developed a standardized data collection form in consultation with clinical specialists, a research methodologist, a statistician, and a social worker, and made appropriate revisions after a pilot of 20 charts. To ensure accuracy of our data abstraction, 25 charts (10%) were abstracted in duplicate by a neutral party. Our agreement on the 20 most important variables was higher than 99%, so we proceeded with 1 data abstractor for the remainder of the charts.

Statistical analysis

We used SAS for Windows, version 9.1, for the analysis. We used frequency tabulations to describe the proportion of women who had 1 or more cervical screening tests in our 3-year study period, to stratify them by the variables in **Table 1**,[22] and to determine the odds ratio for each. The general linear model was used to assess whether or not having 1 or more cervical screening tests was related to each of the variables in **Table 1**.[22]

We used frequency procedures to assess the relationship between having had screening during the study period and having a family physician. We tested the significance of the relative risk using a significance level of $P<.05$.

Frequency procedures were used to determine the proportion of normal and abnormal (atypical

Table 1. Characteristics of HIV-positive women in the cohort: *N* = 218.

CHARACTERISTICS	N (%)	NO. OF WOMEN WITH ≥ 1 CERVICAL SCREENING TEST IN A 3-YEAR PERIOD (%)	OR DESCRIBING THE LEVEL ASSOCIATION BETWEEN SCREENING AND DETERMINANTS (95% CI)
Age at intake, y			
• < 30	64 (29)	47 (73)	reference
• 30-50	141 (65)	73 (52)	0.39 (0.20-0.74)
• > 50	13 (6)	6 (46)	0.31 (0.09-1.05)
HIV-endemic country* (N = 175)			
• Not from endemic country	54 (31)	31 (57)	reference
• From endemic country	121 (69)	76 (63)	1.25 (0.65-2.41)
CD4 cell count at intake, cells/μL (N = 217)			
• < 200	71 (33)	40 (56)	reference
• 200-500	91 (42)	53 (58)	1.08 (0.58-2.02)
• > 500	55 (25)	32 (58)	1.08 (0.53-2.20)
Most recent CD4 cell count, cells/μL			
• < 200	44 (20)	22 (50)	reference
• 200-500	80 (37)	51 (64)	1.76 (0.83-3.71)
• > 500	93 (43)	53 (57)	1.32 (0.64-2.72)
Viral load at intake, copies/mL (N = 217)			
• <500	40 (18)	19 (48)	reference
• 500-5000	75 (34)	52 (69)	2.50 (1.13-5.51)
• 5001-50 000	59 (27)	31 (53)	1.22 (0.55-2.73)
• > 50 000	43 (20)	24 (56)	1.40 (0.59-3.31)
Most recent viral load, copies/mL			
• < 500	137 (63)	88 (64)	reference
• 500-5000	31 (14)	14 (45)	0.46 (0.21-1.01)
• 5001-50 000	29 (13)	16 (55)	0.68 (0.30-1.54)
• > 50 000	20 (9)	8 (40)	0.37 (0.14-0.97)
No. of visits to tertiary care clinic (during 3-y study period)			
• 1	16 (7)	4 (25)	reference
• 2-5	55 (25)	25 (45)	2.50 (0.72-8.72)
• 6-9	46 (21)	22 (48)	2.75 (0.77-9.80)
• > 9	101 (46)	75 (74)	8.65 (2.56-29.20)
OHIP status			
• Not insured by OHIP	26 (12)	8 (31)	reference
• Insured by OHIP	192 (88)	118 (61)	3.59 (1.48-8.67)
Transmission risk group†			
• Heterosexual (N = 216)	208 (96)	121 (58)	2.32 (0.54-9.96)
• IVDU (N = 216)	37 (17)	20 (54)	0.85 (0.42-1.73)
• Blood products (N = 216)	27 (12)	12 (44)	0.55 (0.24-1.24)
• Other (eg, body piercing, tattoo)	31 (14)	16 (52)	0.75 (0.35-1.60)
• Unknown	6 (3)	4 (67)	1.48 (0.26-8.23)

HIV—human immunodeficiency virus, IVDU—intravenous drug user, OHIP—Ontario Health Insurance Plan, OR—odds ratio.

*According to the Public Health Agency of Canada.[22]

†Categories are not mutually exclusive.

squamous cells of undetermined significance, high-grade squamous intraepithelial lesion, low-grade squamous intraepithelial lesion) test results by each woman who underwent cervical screening. Abnormal results are categorized by the highest grade of dysplasia for each woman. The general linear model was used to assess whether abnormal test results were significantly related to the variables in **Table 1**.[22]

Frequency procedures were used to describe the provider performing each test by normal and abnormal test results. We produced contingency tables, χ^2, and *P* values for all other comparisons of proportions. We considered a value of $P < .05$ to be significant.

RESULTS

There were 218 women who met the criteria for inclusion in the cohort, and these women are described in **Table 1**.[22] Although some of the odds ratios in **Table 1**[22] were significant ($P < .05$) for some categories in the general linear model, only the number of visits to the tertiary care clinic and OHIP status were significantly related to the proportion of women receiving cervical screening during the 3-year period (data available upon request).

Ninety-four percent (206 of 218) of the women had primary care providers listed in their medical records. Fifty-eight percent (126 of 218) of the women had at least 1 cervical screening test during the 3-year period. The proportion of women who did not have any cervical tests performed was higher among women who did not have primary care providers (8 of 12 [67%] vs 84 of 206 [41%];

relative risk 1.6, 95% CI 1.06 to 2.52, $P<.05$), but numbers were small in the group without primary care providers.

Thirty-three percent (42 of 126) of the women who underwent cervical screening had at least 1 abnormal test result (**Table 2**). Abnormal results were not significantly related to viral load; however, we found a significant relationship between lower recent CD4 cell count (<200 cells/μL vs ≥200 cells/μL) and having 1 or more abnormal test result ($\chi^2=6.64$, $P=.04$). Abnormal test results were not significantly related to any other characteristic in **Table 1**.[22]

Table 2. Cervical cytology results among 126 women tested: *Only 1 set of results is reported for each woman; abnormal results are categorized by the highest grade of dysplasia for each woman.*

RESULTS	N (%), N = 126
Normal	84 (66.7)
Abnormal	42 (33.3)
• ASCUS	18 (14.3)
• LSIL	27 (21.4)
• HSIL	6 (4.8)
Total	126 (100)

ASCUS—atypical squamous cells of undetermined significance, HSIL—high-grade squamous intraepithelial lesion, LSIL—low-grade squamous intraepithelial lesion.

Primary care providers performed 44% (116 of 262) of all tests and 52% (95 of 181) of the tests with normal results (**Table 3**). Women who had 1 or more abnormal test results were more likely to have had at least 1 cervical screening test performed by an obstetrician-gynecologist (33 of 42 [79%] vs 29 of 84 [34%]; $\chi^2=21.74$, $P<.01$). Women whose test results were all normal were more likely to have had all of their cervical screening tests performed by primary care providers (43 of 84 [51%] vs 8 of 42 [19%]; $\chi^2=12.01$, $P<.01$).

Table 3. Normal and abnormal cervical cytology results by provider specialty: *There were 262 cervical cytology tests among 126 women who received testing.*

SPECIALTY	NORMAL, N (%)	ABNORMAL, N (%)	TOTAL, N (%)
FP	86 (47)	21 (27)	107 (41)
NP	9 (5)	0 (0)	9 (3)
Primary care subtotal	95 (52)	21 (26)	116 (44)
HIV specialist	14 (8)	4 (5)	18 (7)
OBGYN	70 (39)	52 (63)	122 (46)
Other	1 (0.5)	2 (2)	3 (1)
Unknown	1 (0.5)	2 (2)	3 (1)
Total	181 (100)	81 (100)	262 (100)

NP—nurse practitioner, OBGYN—obstetrician-gynecologist.

DISCUSSION

The 3-year cervical screening rate for HIV-positive women in our study (58%) was lower than other reports in the literature.[10-12] However, many studies are based on self-report, which are known to overestimate rates of cervical screening.[23] Rates of cervical screening in women aged 20 to 69 in Ontario are estimated to be 68.6% during a 3-year period,[20] indicating that HIV-positive women might receive less screening than the general population. Our results are strengthened by our ability to study a complete cohort of women and to capture most of the cervical screening results from hospital and community laboratories.

We were not able to detect significant differences in screening rates based on age, country of origin (endemic country), CD4 cell count, viral load, or transmission risk group. The number of tertiary care visits was associated with screening, consistent with an increased opportunity for screening. Women with OHIP coverage were also more likely to receive screening, but because the CytoBase database does not contain women without OHIP numbers, these figures might not include some women who received testing. Therefore, it is difficult to know whether lack of OHIP coverage is truly associated with lower rates of testing.

Other studies have examined factors related to low cervical screening rates for HIV-positive women, including older age, not being white, having less education, being underweight, being obese, being sexually inactive, intravenous drug use, smoking, having a private infectious disease specialist as a care provider, viral load less than 400 copies/mL, and no previous cervical dysplasia.[11] Kaplan and colleagues found that risk factors for lower adherence included white race, intravenous drug use, receiving care for less than 1 year, and 1 or fewer CD4 cell counts performed in the past year.[24] Stein et al found that women who reported having gynecologists and primary care physicians at the same clinical site were almost twice as likely as other women to report receiving Pap testing.[13] Our finding that women from endemic countries do not differ from other women with respect to screening rates requires further investigation in order to ensure that this vulnerable group had adequate access to primary health care.

The prevalence of abnormal Pap smear results among HIV-positive women has been found in other studies to range between 20% and 45%, which is consistent with our results.[25,26] In contrast, the rate of abnormal results among all women in Ontario is 4.5%.[20]

Limitations

First, universal access to health care in Canada, including availability of primary care and specialist physicians, differs from other health care models. Our cervical screening rate is comparable to that found by Keiser et

al among a Swiss cohort, which also reflects a system with universal health care.[11]

Second, this study was performed at a single tertiary care centre; thus, our results might not be generalizable to different HIV care models.

Third, data pertaining to variables such as drug coverage, marital status, language, social support, and living arrangements were inconsistent. Owing to our retrospective design, we were unable to capture other determinants that might have affected attendance for cervical screening among HIV-positive women.

Fourth, we could not access information for women who did not have OHIP numbers (n=26). If the 18 of these women who had no cytological screening recorded received testing at the same rate as those covered by OHIP, our estimate of 3-year screening rate would increase from 58% to 61%.

Finally, the criteria used to determine the presence of a primary care physician (ie, listed on a dictated consultation note, a referral form, or any other documentation) might overestimate the proportion of patients receiving primary care. We administered a questionnaire to a subset of women (n=78) to more accurately determine the proportion of women receiving primary care. Only 59 (76%) women reported having primary care providers, despite 97% (76 of 78) of these women having primary care providers listed in their charts. Of the women surveyed, 71% (55 of 78) had undergone cervical screening in the past 3 years (compared with 58% of the total cohort). However, this group differed in a number of characteristics that would prevent us from making generalizations to the full cohort.

In another study of HIV-positive women, 93% reported having primary care providers.[27] However, primary care providers were defined as "one provider that you see for most (more than half) of your medical appointments," which could be a tertiary care specialist managing HIV rather than all preventive and promotional health services. Meyerson et al found that white patients, women exposed to HIV through heterosexual sex, and those with a diagnosis of AIDS were more likely to receive primary medical care than other HIV-positive patients were.[28] However, this study defined utilization of HIV primary medical care as evidence of CD4 cell count or viral load measurement, an HIV primary care service visit, or use of HIV medications. This indicates that we need a better method of assessing whether HIV-positive women are adequately accessing the full spectrum of primary and preventive health services available to women not infected with HIV.

Conclusion

Our results support our hypothesis that HIV-positive women who do not have primary care providers are less likely to undergo cervical screening. We found that primary care providers performed more of the cervical cytology tests with normal results, which might indicate that family physicians are performing routine preventive health care for HIV-positive women. Current therapies have greatly decreased the morbidity and mortality associated with HIV infection, and HIV-positive women deserve the same standard of care to prevent comorbid illness as their counterparts who are not infected with HIV.[9] Future research should be directed toward optimizing access to and quality of primary health care for this population.

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Contributors

Dr Leece contributed to acquisition of data, analysis and interpretation of data, and drafting and critical revision of the manuscript. **Dr Kendall** contributed to conception and design of the study, obtaining funding, supervision, and drafting and critical revision of the manuscript. **Dr Touchie** contributed to conception and design of the study and critical revision of the manuscript. **Dr Pottie** contributed to conception and design of the study and critical revision of the manuscript. **Dr Angel** contributed to the concept and design of the study, data collection and analysis, and critical revision of the manuscript. **Mr Jaffey** contributed to statistical analysis and critical revision of the manuscript.

Competing interests

None declared

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