Invasive Cervical Cancer Among American Indian Women in the Northern Plains, 1994–1998: Incidence, Mortality, and Missed Opportunities

Richard F. Leman, MD[a]
David Espey, MD[b]
Nathaniel Cobb, MD[c]

SYNOPSIS

Objectives. Cervical cancer mortality rates among the American Indian and Alaska Native (AI/AN) population in North and South Dakota were five times the national average (15.6 per 100,000 vs. 3.1 per 100,000, age adjusted) when last evaluated (from 1989 through 1993). Our goals were to update the AI/AN population cervical cancer mortality rates and to present incidence rates for AI/AN women in the region.

Methods. We reviewed charts for women diagnosed with invasive cervical cancer at Indian Health Service (IHS) facilities in North and South Dakota from 1994 through 1998 and collected information about cervical cancer screening and treatment history. Incidence and mortality rates were standardized to the 1970 U.S. population.

Results. Twenty-one cases of invasive cervical cancer and eight deaths were identified. Annualized incidence and mortality rates were 11.5 per 100,000 and 4.5 per 100 000. These compare with national all-race/ethnicity rates of 8.5 per 100,000 and 2.7 per 100,000 for incidence and mortality. Fifteen (71%) of 21 cases were diagnosed due to symptoms.

Conclusions. While cervical cancer mortality rates have declined, incidence and mortality rates among AI/AN women remain higher than in the general U.S. population. Increased use of pap tests and careful follow-up of abnormal results should be aggressively promoted among AI/AN women in North and South Dakota.

[a]Oregon Health Services/Health Promotion and Chronic Disease Prevention Program, Portland, OR; at the time of this study, Dr. Leman was with the Epidemic Intelligence Service, Division of Applied Public Health Training, Epidemiology Program Office, Centers for Disease Control and Prevention, Atlanta, GA; National Epidemiology Program, Indian Health Service, Albuquerque, NM

[b]National Epidemiology Program, Indian Health Service, Albuquerque, NM; Epidemiology and Health Services Research Branch, Division of Cancer Prevention and Control, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, GA

[c]National Epidemiology Program, Indian Health Service, Albuquerque, NM

Address correspondence to: Richard F. Leman, MD, Oregon Health Services/Health Promotion and Chronic Disease Prevention Program, 800 NE Oregon St., Ste. 730, Portland, OR 97232-2162; tel. 503-731-4273; fax: 503-731-4082; e-mail <Richard.f.leman@state.or.us>.

Invasive cervical cancer is an important and largely preventable cause of morbidity and mortality among women.[1,2] Regular, periodic screening of cervical cytology through the use of Papanicolaou (pap) testing has been associated with decreased risk of developing invasive cervical cancer and is widely recommended.[3–6] Numerous studies have demonstrated that invasive cervical cancer incidence rates among the American Indian and Alaska Native (AI/AN) population are higher than among the white population.[7–12] Two studies found that cervical cancer incidence rates among AI/AN women substantially increased when racial misclassification of AI/AN case subjects was corrected.[7,13] Other assessments have noted higher AI/AN mortality rates from invasive cervical cancer.[10,11,14] An Indian Health Service (IHS) internal study demonstrated cervical cancer mortality rates among AI/AN women seen at IHS facilities in North Dakota and South Dakota from 1989 through 1993 (15.6 per 100,000; 95% confidence interval [CI] 9.9, 24.6, age adjusted) to be five times the national average (2.9 per 100,000; 95% CI 2.9, 3.0, age adjusted).[15] We reevaluated mortality rates for invasive cervical cancer among AI/AN women seen at IHS facilities in North and South Dakota (the study population) from 1994 through 1998 and, for the first time, determined cervical cancer incidence rates in this population. The study further assessed the patterns of screening and follow-up care among AI/AN women diagnosed with this condition.

METHODS

Data sources for incidence rate calculation

To identify cases of invasive cervical cancer in the study population, we conducted an electronic search using the Resource Patient Management System (RPMS), an electronic data storage and retrieval system widely available in IHS and tribal health facilities.[16] Patients are entered into the RPMS system when they first register for care at a facility and document their eligibility (i.e., by proving tribal membership). All IHS and tribal health care facilities located in North Dakota and South Dakota were included in the search. *International Classification of Disease, Ninth edition, Clinical Modification* (ICD-9-CM) codes 180.0, 180.1, 180.8, and 180.9 were used to identify all cases of invasive cervical cancer diagnosed among individuals receiving care at the included facilities from January 1, 1994, through December 31, 1998 (the study period).[17] (See Table 1.)

Table 1. ICD-9-CM codes used in electronic database search, Indian Health Service, Aberdeen Area, 1994–1998

ICD-9-CM code	*Definition*
180.0	Malignant neoplasm of the endocervix
180.1	Malignant neoplasm of the exocervix
180.8	Malignant neoplasm, other specified sites of cervix
180.9	Malignant neoplasm of cervix, unspecified

ICD-9-CM = *International Classification of Disease, Ninth Revision–Clinical Modification*

We also reviewed Contract Health Services records for all IHS facilities in North and South Dakota for the study period using as search criteria the same ICD-9-CM codes. These records contain information about all IHS-funded care at non-IHS facilities, including visits for cervical cancer diagnosis and treatment. We removed duplicate entries from the resulting lists and reviewed the medical chart for each identified woman to confirm the diagnosis.

For the denominator, we used the mid-period (1996) IHS service population for North Dakota and South Dakota (the Aberdeen Area). The *service population* is composed of those individuals residing in the *IHS Service Area* (i.e., in counties identified by the Census Bureau as being on or near reservation lands) who identified themselves as American Indian, Eskimo, or Aleut during the U.S. Decennial Census. The IHS Service Area represented 80% of all self-identified AI/ANs in North Dakota and 89% of all self-identified AI/ANs in South Dakota, according to Census figures. The U.S. Census Bureau intercensal estimate of the North and South Dakota IHS service population for 1996 was used.[18]

Data sources for mortality rate calculation

The total number of invasive cervical cancer deaths among AI/AN women in North and South Dakota during the study period was determined through review of National Center for Health Statistics mortality tapes.[19] The search was limited to counties included in the IHS Aberdeen Service Area in order to (*1*) decrease the likelihood of racial misclassification, (*2*) be consistent with the method used in the previous analysis of cervical cancer mortality in the region, and (*3*) facilitate comparison with incidence rates calculated in this study.[15] For the denominator, we again used the 1996 intercensal estimates of the AI/AN population in those same counties.

Data collection for assessment of screening and treatment history

Through chart review, we also collected information about cervical cancer screening and treatment history. Data were collected using a standardized form. We recorded demographic information (age at diagnosis, race/ethnicity, facility at which diagnosis was made) and data on potential risk factors (e.g., history of human papilloma virus infection) and associated risk behaviors (e.g., documentation of alcohol abuse.) History of tobacco use was not assessed because of difficulty obtaining complete information about this characteristic during previous chart reviews. We also collected information regarding the timing and mode of diagnosis and treatment (i.e., date of diagnosis, stage at diagnosis, whether diagnosis was prompted by symptoms or by screening, date of cervical biopsy, and start date and nature of treatment). We then evaluated screening history by documenting age at first pap test, and the results and follow-up for the three most recent pap tests preceding the diagnosis. Evidence of cervical cancer screening at non-IHS facilities was sought and any available records of such care were reviewed.

Analysis

Incidence and mortality rates were age-adjusted using the 1970 U.S. standard population. The incidence rate then was compared with age-adjusted national all-race/ethnicity data obtained through the Surveillance, Epidemiology, and End Results Cancer Registry System (SEER) using SEERStat CD.[20] Published SEER data for AI/AN population-specific cancer incidence are available only for New Mexico.[21] Mortality data demonstrate that the pattern of cancer in AI/AN populations varies by geographic region, making extrapolations from New Mexico data problematic.[14] Further, the last published mortality data cover the period from 1988 through 1993, before our study period.[14,15] For these reasons, they were not included for comparison.

Statistical analysis was conducted using Epi-Info 6.04 software and SAS 8.2 software.[22,23] Proportions were compared using the chi-square or two-tailed Fisher Exact test. Relative risks (RRs) were obtained, and 95% CIs were subsequently calculated.[24] The Exact Mann-Whitney test was used to compare medians of independent continuous samples.

RESULTS

Twenty-one cases of invasive cervical cancer diagnosed during the study period were confirmed by chart review. The annualized, age-adjusted incidence rate was 11.5 per 100,000 (95% CI 7.3, 18). This compares with an incidence rate of 8.5 per 100,000 for the SEER program (7.9 per 100,000 for non-Hispanic white women). The age-adjusted mortality rate from invasive cervical cancer in the Aberdeen Service Area was 4.5 deaths per 100,000 (95% CI 2.2, 9.4) during the study period. The mortality rate from invasive cervical cancer in the U.S. general population for the same period was 2.6 deaths per 100,000 (95% CI 2.6, 2.7).

Table 2 presents the characteristics of women diagnosed with invasive cervical cancer during the study period. All were identified as AI/AN. The median patient age was 39 years (mean=46 years; range=24–82 years). Five (24%) of 21 patients were diagnosed as a result of findings on a screening pap smear, and 15 (71%) were diagnosed after presenting with symptoms. Mode of diagnosis could not be determined for one person (5%). (See Table 2).

Six (28%) of 21 patients had Stage I disease at the time of diagnosis, and three of these patients (14%) had microinvasive findings on biopsy. Thirteen patients (62%) had Stage II or higher at diagnosis, and staging at diagnosis was not documented for two patients (10%).

Fourteen (67%) of 21 patients had a pap smear documented in the chart at some time before their invasive cervical cancer diagnosis. The median time between the most recent pap test and cancer diagnosis was 362 days (mean=1,522 days). Of five women diagnosed as a result of pap screening, three had a delay of more than 100 days from the pap test to cervical cancer diagnosis (median delay for the group diagnosed by screening=116 days; range 0–224 days.) Women with prior pap screenings whose diagnosis was based on symptoms had a median of 1,732 days between their most recent pap test and diagnosis (range=14–7,153 days). The difference in time from pap test to diagnosis in the two groups was statistically significant (p=0.039).

Table 2. Characteristics of 21 AI/AN women diagnosed with invasive cervical carcinoma, Indian Health Service, Aberdeen Area, 1994–1998

Characteristics	n *(range or percent)*
Demographics	
Median age at diagnosis	39 (24–82 years)
Potential risk factors	
Previous alcohol use	10 (48%)
Current alcohol use	4 (19%)
History of HPV	0 (0%)
History of chlamydia	3 (14%)
History of gonorrhea	1 (5%)
History of PID	2 (10%)
History of other STD	4 (19%)
Diagnosis/screening	
Stage at diagnosis:	
I	6 (28%)
II	6 (28%)
III	4 (20%)
IV	3 (14%)
Unknown	2 (10%)
Mode of diagnosis	
Screening pap	5 (24%)
Presence of symptoms	15 (71%)
Unknown	1 (5%)
Colposcopy scheduled	16 (76%)
Treatment	
Start of treatment documented	20 (95%)
Median number of days from diagnosis (n=20)	31 (0–359 days)

AI/AN = American Indian/Alaska Native

HPV = human papilloma virus

PID = pelvic inflammatory disease

STD = sexually transmitted disease

Of 16 women who had a scheduled colposcopy date documented in the chart, 13 (81%) kept the scheduled appointment. For the 20 women whose treatment start date could be determined, the median time between diagnosis and treatment was 31 days (range=0–359 days). The mean was 65 days.

Women who had a diagnosis of cervical cancer as a result of pap screening were less likely to have advanced stage disease at diagnosis, but the association was not statistically significant (RR=0.3; p=0.08). The median time from diagnosis to treatment for those diagnosed on the basis of presence of symptoms was 31 days, for those diagnosed by screening, it was 172 days. (Exact Mann-Whitney p-value=0.55) One of nine women aged ≥50 years was diagnosed through screening compared with four of 11 younger women.

DISCUSSION

This study is noteworthy for two key findings. First, more than two-thirds of the women with cervical cancer during

the study period were diagnosed because of symptoms, not through screening. Second and more encouraging, the mortality rate for invasive cervical cancer among AI/AN women in North Dakota and South Dakota has declined significantly since last evaluated. Further, although the mortality rate is still 1.7 times higher than that in the general U.S. population, the difference is not statistically significant.

This is the first time that the cervical cancer incidence rate has been calculated for the study population. Although this rate was higher than that in the general U.S. population, the difference again did not reach the level of significance. This is at least in part due to the small numbers of AI/AN women affected by cervical cancer in this sparsely populated area, and the resultant wide CIs. Previous studies demonstrating higher incidence rates among AI/AN and Canadian First Nation communities than among the general population living in the same region used data from several years before the current investigation.[7–12,25] The current findings suggest that, while the disparity in cervical cancer morbidity and mortality between AI/AN women and women in the general population is narrowing, this disparity has not been eliminated.

Several possible explanations have been proposed for the higher cervical cancer incidence rates noted among AI/AN women. One study reported the development of an "interval cancer" (no prior dysplasia and a negative screening report within three years of diagnosis) in 23 (52%) of 44 AI/AN women with invasive cervical cancer whose charts were reviewed.[26] Such cases of "missed diagnosis" have been attributed to failure at the time of interpretation to recognize smears with inadequate cellular material and, less commonly, to missed diagnosis of dysplasia on an adequate smear.[27–29] A rapidly progressive variant of cervical cancer has been hypothesized but has not been well documented.[30,31]

A more likely explanation involves the low prevalence of cervical cancer screening often seen in AI/AN populations. Recent studies in the Northern Plains have found that 26% to 33% of AI/AN women with diabetes had had a pap smear within a 12-month period and that the average for all IHS areas was 42%.[32,33] Low rates of screening can allow precancerous lesions to progress to invasive cancer before they are detected. Government Performance Review Act data for the IHS Aberdeen Area show rates for annual pap screening of 40.5% in 1998, 40.9% in 1999, and 40.7% in 2000 (Personal communication, Tracey Lynn, IHS Aberdeen Area, October 2001). While describing findings from the National Breast and Cervical Cancer Early Detection Program, one study reported that AI/AN women were more likely to report never having had a pap test and that AI/AN women had the highest proportion of abnormal results on their first screening pap tests through the program.[34] Further, 55% of AI/AN women with invasive cancer had no history of prior pap screening.[34]

Although rates of screening (history of at least one pap prior to diagnosis) in our study were somewhat higher (67%), our findings suggest that regular, repeated screening could facilitate earlier diagnosis. The significantly shorter interval from last pap test to diagnosis through screening vs. diagnoses through symptoms suggests that regular screening in the latter group could have permitted more rapid detection of disease. The median delay between diagnosis and treatment of almost six months among women diagnosed through screening is also a concern and raises the question of whether more expeditious treatment could have decreased morbidity and mortality in this group.

This investigation had several limitations. We did not have access to information about cervical cancer cases among AI/AN women seen exclusively at non-IHS facilities. This is a potential source of selection bias and could result in inappropriately low calculated rates of cervical cancer incidence and mortality. Because those eligible for IHS care can receive it at any IHS facility, a possibility exists that some of the women identified with cervical cancer through this study lived outside the study area and were visiting North or South Dakota at the time of the clinic visit. However, presence of a confirmatory cervical biopsy was documented for all cases in the IHS medical record, so it appears unlikely that any such "drop in" visitors are included among the cases identified.

Another possibility is that women diagnosed with cervical cancer at IHS clinics could have received cervical cancer screening services at other facilities, with no record of this in the IHS chart. This could lead to underestimation of the frequency of such screening among women with cervical cancer identified in our study. However, given the long distances to alternative health facilities in this largely rural study area and the extent of poverty among reservation residents, such use of other screening resources is likely to be low. Records were obtained from private sector physicians when such screening was known to have occurred. Incomplete documentation of previous pap smears or cervical biopsy results in IHS charts may have resulted in information bias. Omission of appropriate ICD-9-CM codes from the electronic records of women with invasive cervical cancer could have introduced case-ascertainment bias, resulting in an artificially low incidence rate. Also, because of the small absolute number of invasive cervical cancer cases among AI/AN women in the Northern Plains, CIs are wide enough that they overlap all-race/ethnicity rates for incidence and mortality calculated from SEER data. Therefore, the difference between AI/AN population rates and SEER-based all-race/ethnicity rates is not statistically significant.

Delay in diagnosis of cervical neoplasia until invasive cancer has developed clearly increases potential mortality from the condition. No previous studies have evaluated frequency of presentation with advanced stage disease among the AI/AN population. Our findings that more than 60% had Stage II disease or higher at diagnosis, coupled with elevated mortality rates, strongly underscore the need for more aggressive screening in this population.

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