International Journal of Tropical Medicine 1 (1) : 6-10, 2006

Epidemiology of Cervical Cancer and Dysplasia in a Cross-Sectional Study of Women in Accra, Ghana

[1]Grace, L.C., [2]G.H. Allan, [3]S. Joseph, [4]M.K.A. Richard, [5]D. Rudolph,
[6]K.A. John and [7]B.D. Rosemary
[1]Department of Medicine ,[2]Department of Surgery, Beth Israel Deaconess Medical Center, Harvard Medical School, 330 Brookline Avenue, Boston, MA. 02215
[3]Department of Population and International Health, Harvard School of Public Health, 677 Huntington Avenue, Boston, MA. 02115
[4]Department of Surgery,
[5]Department of Obstetrics and Gyneacology
[6]Department of Obstetrics and Gyneacology, Korle Bu Teaching Hospital
[7]Institute for Statistical, Social and Economic Research, University of Ghana, Accra, Ghana

Abstract: A comprehensive study of women living in Accra, Ghana was conducted to determine the burden of disease of communicable and non-communicable illnesses in urban women in a developing country. Incorporated in that evaluation was an assessment of the prevalence of cervical cancer and dysplasia. Medical interviews and physical examinations with Papanicolaou smears were performed for 843 women residing in metropolitan Accra. The prevalence of cervical cancer detected was 0%; HGSIL 0.5%; LGSIL 0.4% and atypia 7.3%. Women with an abnormal Pap smear were more likely to have had a stillbirth (OR 1.35 [1.02-1.79], p = 0.037] compared to women with a normal result. Only 26 women (1.9%) reported a prior Pap smear. There was no association with known risk factors including age at first intercourse, unprotected sexual intercourse, diagnosis or symptoms of sexually transmitted diseases, HIV status, number of lifetime partners, or income with Pap smear result. It was anticipated that a significant number of women would be diagnosed with cervical cancer and cervical dysplasia. The explanation for the unexpectedly low number of cases of cervical dysplasia and cancers is not evident. These results may underestimate the magnitude of this health condition or they may represent the true burden of the cervical dysplasia in this particular urban population at this time. Further studies are needed to differentiate these two possibilities.

Key words: Cervical cancer, screening, west africa, sub-saharan, Africa

INTRODUCTION

Cervical cancer is the second most common malignancy affecting women worldwide[1]. The Papanicolaou (Pap) smear has been recognized as the most effective cancer screening test developed[2]. Screening for cervical cancers by the Pap smear has resulted in a substantial decrease in the incidence and mortality from cervical cancer in the USA and Western Europe[3-6]. Few developing countries have the resources necessary to embark on a large scale cervical cancer program, yet the majority of women afflicted with cervical cancer reside in these areas[7].

The Women's Health Study of Accra (WHSA) was conducted in 2003 to assess the magnitude of the burden of disease of communicable and non-communicable illnesses in urban adult women residing in the greater metropolitan area of Accra, Ghana, West Africa. Included in this study was the opportunity to have a Papanicolaou (Pap) smear performed for screening for cervical cancer. The primary objective of this analysis is to determine the prevalence of cervical cancer among this population of women and to describe demographic and clinical characteristics associated with abnormal findings on Pap smears.

MATERIALS AND METHODS

Study site and sampling design: According to the March 2000 census, the Greater Accra Metropolitan Area is inhabited by 1.66 million people, 365,550 households and 839,310 women (50.6%). This is an economically and culturally diverse area[8]. The sampling design is described in detail and was comprised of two stages: 1) the selection

Crossponding Author: Rosemary, B.D., BIDMC RW 871 330 Brookline Avenue Boston, MA. 02215 U.S.A.
Tel: 617-667-2169 Fax: 617 667 2978

Table 1: Descriptive Characteristics for the Demographic Characteristics of Women Who Was Screened for Cervical Cancer with Pap Smear (N = 843 Total)

Demographic Characteristic	Pap smear Performed (n/%)
Age (yrs)	
Mean/ S.D	45.62±17.5
Range	18-100
Socioeconomic status % (No)	
Low	24.9 (210)
Low middle	27.2 (229)
High middle	26.6 (216)
High	22.3 (188)
Total	100 (843)
Monthly income % (No)	
Less than 300,00	29.5 (191)
300,000-500,000	27.2 (176)
500,000-1,000,000	32.9 (213)
1,000,000-5,000,000	10.5 (68)
Total	100 (648)
Level of education % (No)	
No education	30.2 (250)
Primary	9.2 (76)
Middle	42.1 (348)
Secondary	11.6 (96)
Higher	6.9 (57)
Total	100 (827)
Work status % (No)	
Formal employment	10.0 (83)
Self-employed	54.7 (456)
Student or apprentice	5.0 (42)
Housewife	2.9 (24)
Retired	2.4 (20)
Unemployed	25.1 (209)
Total	100 (834)
Ethnicity % (No)	
Akan	31.3 (262)
Ga	44.5 (372)
Ewe	11.5 (96)
Guan	0.2 (2)
Mole-Dagbani	1.6 (13)
Grussi	0.6 (5)
Hausa	3.1 26)
Other	7.2 60)
Total	100 (836)

of the Enumeration Areas and 2) the selection of eligible women[9,10]. Eligible women for this study included those that are usually resident in the greater Accra metropolitan area, age 18 years of age and older, non-incarcerated and available to answer survey questions at home and in the gynecologic clinic at the university teaching hospital. The women in the WHSA are a representative socioeconomic and ethnic sampling of the adult women residing in Accra based on the information from the 2000 census. The study was designed to utilize the usual local cervical cancer screening resources.

Data collection: A comprehensive history, physical and laboratory examination (CMLE) was performed approximately one month following the household survey at the gynecology out-patient clinic at Korle Bu Teaching Hospital, University of Ghana, Accra. The CMLE were performed by the university physicians. Pap smears were taken by swabbing the cervical os and the posterior vaginal fornix.

The pathologists at Korle Bu Teaching Hospital examined the prepared slides and categorized the results as follows: 1) No dyskariosis; 2) enlarged nuclei, no dyskariosis; 3) Enlarged nuclei, with dyskariosis; 4) Mild dysplasia - CIN I; 5) Moderate dysplasia - CIN II; 6) Moderate dysplasia - carcinoma-in-situ - CIN III and 7) invasive cancer.

For our analysis, these categories were reclassified into the more widely used Bethesda staging nomenclature[11]. Enlarged nuclei without dyskariosis were considered to be equivalent to atypia using the ASCUS/ASGUS category; enlarged nuclei with dyskariosis and CIN I were re-classified as low grade squamous epithelial lesions (LGSIL); CIN II and CIN III are regrouped into high-grade squamous epithelial lesions (HGSIL).

Statistical analysis: Data was entered into SPSS version 13 database and SAS version 8 for windows. Statistical analysis was performed using descriptive frequencies, logistics, Student t-Test two-sided testing and nonparametric analyses including Wilcoxan Rank Sum Test, Fisher's Exact Test and Chi-square analysis, when appropriate. The Odds Ratio (OR) with a 95% Confidence Interval (CI) was used to describe the strength of the association. Statistical significance was defined as $p< 0.05$.

Institutional review board approval: This study was approved by the Human Subjects Committee at Harvard School of Public Health, Noguchi Memorial Institute for Medical Research, University of Ghana and data analysis approved by the Beth Israel Deaconess Medical Center. Informed consent was obtained prior to the HHS, CMLE and HIV testing.

RESULTS

The demographic characteristics of the patients are provided in Table 1. A total of 3175 women were interviewed at home and 1328 of those women were examined in the outpatient clinic. The women were allowed to opt out of any portion of the study.

There were 860 Pap smears obtained. The quality of 20 smears was judged to be unsatisfactory, however 6 were interpreted diagnostically. Three additional smears were not read due to multi-layering of the cells. Hence, a total of 843 slides were diagnostically interpreted.

Among the women in Accra who participated in the study and had a Pap smear performed, the mean age was 45.62±17.5, age range 18-100. Figure 1 shows the age

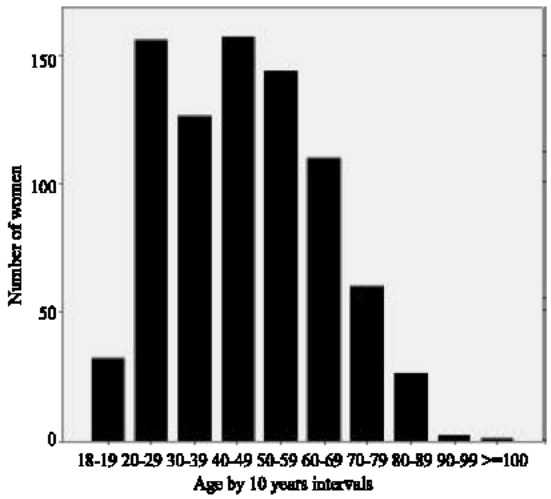

Fig. 1: Age of women by decade screened for cervical cancer

distribution by decade of the women who had a pap smear performed. Women were equally distributed among four socioeconomic classes and approximately 90% of women reporting income made less than 1,000,000 cedis per month (approximately 125 USD). Approximately 70% of women reported having some level of education- 42% reported having completed middle school, 11.6% reporting having completed secondary school and 6.9% reported having completed a higher level of education. The majority of women who obtained Pap smears in our study described themselves as Ga (44.5%) or Akan (31.4%).

The prevalence of cervical dysplasia and cancer that were determined by the Pap smears are displayed in Table 2. Based on the results of all recorded Pap smears, 90.1% of women had normal smears. 8.7% were classified as atypical, 0.6% as LGSIL, 0.6% were diagnosed as HGSIL. There were no detected cases of cervical cancer in our population. Of the 6 smears judged to be of unsatisfactory quality, 5 were read as normal and one as LSGIL. The mean age of the women with a normal Pap smear was 45.6±17.7 years compared to 44.9±18.0 years for those with atypia (p=ns); 58.8±6.4 years for those with LGSIL (p=0.01) and 57.0±17.8 years for those with HGSIL (p=ns).

Table 3 shows the results of the Pap smears compared to the results of the internal pelvic examination findings. There were 10 women (1.2%) who had a suspicious finding on the internal pelvic examination, but all had a normal Pap smear report. Of the 34 women (4.0%) who had bloody non-menstrual cervical discharge, 31 had a normal Pap smear, 2 had atypia and 1 had HGSIL reported. Of the 20 women who had an unsatisfactory quality Pap smear, 13 had a normal internal examination recorded, 2 had bloody cervical discharge, 3 had non-bloody cervical discharge 1 had an ulcerated cervix and 1 had a clinically suspicious cervical lesion identified. Of the 6 women with an unsatisfactory quality Pap smears and a diagnostic report, 3 had a normal pelvic examination (including the one with HGSIL) recorded and one each had bloody cervical discharge, ulcerated cervix and non-bloody cervical discharge recorded.

There were no significant demographic differences in age, area of residence, ethnicity, religion, socioeconomic status of the EA, income or highest education level attained between women who had a normal Pap smear compared with all others with an abnormal Pap smear. There were also no statistically significant differences for age at first intercourse, age at first delivery, adjusted lifetime number of sexual partners, unprotected sexual intercourse, past history of Sexually Transmitted Infections (STIs) or current symptoms suggestive of STIs, lifetime number of partners, HIV status[12], or previous cervical cancer screening. A detailed reproductive health history revealed a significant association between an abnormal Pap smear and a history of stillbirths (OR 1.35 [1.02-1.79], p = 0.37 but no statistically significant association with a history of miscarriages or induced abortions.

DISCUSSION

Cervical cancer is the most prevalent gynecologic malignancy in Sub-Saharan Africa (SSA)[13-16]. The annual number of new cases worldwide is estimated to be approximately 500,000[17]. The risk of developing cervical cancer in the developing world before age 65 is 1.5%. One retrospective study conducted by Nykekyer in 2000 described the cervical cancer prevalence rate of 1.6% among Ghanaian women admitted to the gynecologic unit at Korle Bu Teaching Hospital[18]. This hospital based study represented women who were referred to the unit from all areas of Ghana, not just Accra.

The age-specific prevalence rate of cervical cancer in an unscreened population was reported in a South African investigation[19]. The average age for those diagnosed with cervical cancer was 51.3 years, significantly higher than those diagnosed with LGSILs (33.1 years) or HGSILs (38.0 years). A clear relationship was found with young age and LGSILs and older age and invasive cancer. These data indicate that cervical cancer is a common disease and that it is a disease of older women in an unscreened women residing in developing countries. The mean age of women in the WHSA with LGSILs and HGSILs was higher than reported in the South African study.

Table 3: Results of Internal Examination Compared to Pap Smear Results by the Bethesda Classification

		% (No)	Pap Smear Results n		
Internal Exam finding		Normal	Atypia	LSGIL	HGSIL
Normal	68.0(573)	516	51	4	2
Abnormal vaginal mucosa	1.5(13)	12	1	0	0
Adnexal or parametrial mass	0.4(3)	3	0	0	0
Enlarged uterus, not pregnant	1.9(16)	13	3	0	0
Uterine fibroids	1.4(12)	9	3	0	0
Uterus enlarged, pregnant	0.6(5)	4	1	0	0
Ulcerated cervix	0.7(6)	5	1	0	0
Cervical tenderness	0.9(8)	8	0	0	0
Cervical discharge, bloody	4.0(34)	31	2	0	1
Cervical discharge, nonbloody	7.1(60)	55	5	0	0
Cervical erosion	1.2(10)	9	0	0	1
Cervical lesion, non-cancerous	2.8(24)	21	2	1	0
Cervical lesion, cancer/tumor	1.2(10)	10	0	0	0
Other, probably benign	5.0(42)	8	4	0	0
Pelvic Exam not recorded	3.2(27)	26	0	0	1
Total	843	760	73	5	5

In a country with limited resources for health care and public health services, cervical cancer screening has not been an apparent major public health priority in Ghana, based on the few women who recall ever having had a previous Pap smear in this study. In a previous report we describe the paucity of cervical cancer testing performed for these women[20]. The unexpected findings of this present report are the very few cases of cervical dysplasia and no cervical cancers identified despite the absence of routine cervical cancer screening of any type in this population.

The most common abnormality reported by cervical cytology is atypical squamous cells (ASC)[21]. Our study supported that finding with ASC being identified in 73 of 83 women (87.9%) with an abnormal examination.

Based on these estimations from the literature for SSA, it was expected that 20 women would have been identified with low-grade dysplasia (LGSILs in the Bethesda Classification), 15 women with high-grade lesions and 8 with a cervical cancer. Based on these rates, our inability to detect any cases of cervical cancer is statistically significant from the expected rates previously noted ($p<0.001$).

Our results may be explained in part by selection bias of the study sample, experience and technique in obtaining the cervical samples, a decreased sensitivity of the test or that the findings of this study represents the true prevalence of cervical dysphasia in this population. Selection bias of entering women in this study is unlikely as they were randomly selected to be a representative sampling of all adult women residing in Accra.

In this university institution where the study was conducted, training in cervical cancer screening techniques is included early in the course of medical student and resident education. Screening by the visual inspection and acetic acid technique is also performed, however, there are no published accounts of the frequency of routine use nor the detection rate of cervical dysplasias or cancers in this population. The physicians who performed most of the pap smears were in training and this may have contributed to the number of women who had an unsatisfactory smear submitted for review. Another reason for the low detection of cervical dysphasia may be the inability to detect cervical dysplasia and cancer within our Ghanaian population. Even within institutions that routinely conduct screening, the sensitivity of a single Pap smear in detecting cervical cancer is in the range of 60%[22] and intraepithelial lesions are likely underestimated in approximately 17.5% of cases according to previous studies[23]. Screening for cervical cancer by adding human papillomavirus (HPV) DNA testing and triage rather than utilizing Pap smears alone should be considered and may in the long run be more cost-effective than cytology based screening programs alone[24].

Also unexpected was the lack of a significant association of an abnormal Pap smear with known risk factors for cervical cancer including poverty, age at first intercourse, unprotected sexual intercourse and a diagnosis or symptoms of sexually transmitted infections. The lack of a statistical association with known risk factors for cervical cancer can be explained by the few cases of cervical dysplasia identified.

An alternative explanation for the findings of the WHSA may be that these low prevalence rates are accurate among women in Accra due to factors that were not examined in our study. Certainly, previous studies have shown great variation among cervical cancer prevalence within Africa- women in Egypt have been noted to have rates comparable to European women despite lack of screening. (7)[25]. While the causes for this variability among African women have not been

determined, they could certainly include other demographic characteristics as well as behavioral and biologic factors (e.g., high-risk HPV genotype prevalence) that we did not investigate. Future prospective trials to compare these factors in the development of cervical dysplasia and cancer would help us to understand barriers in screening and improve our ability to decrease rates among African women.

REFERENCES

1. Parkin, D.M., F. Bray, J. Ferlay and P. Pisani, 2005. Global Cancer Statistics. CA Cancer J. Clin., 55: 74-108.
2. Felix, J.C. and C. Amezcua, 2002. *In vitro* adjuncts to the Pap smear. Obstet Gynecol Clin. North Am., 29: 685-99.
3. Devesa, S.S., D.T. Silverman, J.L. Young Jr, E.S. Pollack, C.C. Brown, J.W. Horm, C.L. Percy, M.H. Myers, F.W. McKay and J.F. Fraumeni Jr, 1987. Cancer incidence and mortality trends among whites in the United States, 1947-84. J. Natl. Cancer Inst., 79: 701-7.
4. Bray, F., A.H. Loos, P. McCarron, E. Weiderpass, M. Arbyn, H. Moller, M. Hakama and D.M. Parkin, 2005. Trends in cervical cancer squamous cell carcinoma incidence in 13 European countries: changing risks and the effects of screening. Cancer Epidemiol Biomarkers Prev., 14: 677-86.
5. Johannesson, D., G. Geirsson and N. Day, 1978. The effect of mass screening in Iceland, 1965-74, on the incidence and mortality of cervical carcinoma. Int. J. Cancer, 21: 418-25.
6. Sherman, M.E., S.S. Wang, J. Carreon and S.S. Devesa, 2005. Mortality trends for patients for cervical squamous and adenocarcinoma in the United States: Relation to incidence and survival. Cancer, 103: 1258-1264.
7. Reichenbach, L., 2002. The politics of priority setting for reproductive health: Breast and cervical cancer in Ghana. Repro. Health Matters, 10: 47-58.
8. Songsore, J. and G. Goldstein, 1996. Wealth, health and the urban household. Chapter 8 in: Urban health research in developing nations Oxford, CAB International.
9. Megill, D., 2002. Recommendations for designing master sample for Ghana intercensal household survey program Ghana Statistical Service and U.S. Bureau of Census.
10. Hill, A.G., A.G. Hill, J. Anarfi, R. Darko, R.M.K. Adanu, J. Seffah and R.B. Duda, 2005. Measuring population health: The design and conduct of women's health in Accra, Ghana. Submitted to WHO Bulletin.
11. National Cancer Institute Workshop, 1989. The 1988 Bethesda System for reporting cervical/vaginal cytological diagnoses, JAMA, 262: 931-934.
12. Duda, R.B., R. Darko, R.M.K. Adanu, J. Seffah, J.K. Anarfi , S. Gautam and A.G. Hill, 2005. HIV prevalence and risk factors in women in Accra, Ghana: Results from the Women's Health Study of Accra. In press, AJTMH.
13. Rogo, K.O., J. Omany, J.N. Onyango, S.B. Ojwang and U. Stendahl, 1990. Carcinoma of the cervix in the African setting. Int. J. Gynec Obstet, 33: 249-55.
14. Kasule, J., 1989. The pattern of gynecologic malignancy in Zimbabwe. East Afr. Med. J., 66: 393-9.
15. Emembolu, J.O. and C.C. Ekkwempu, 1988. Carcinoma of the cervix uteri in Zaria: Etiologic factors. Int. J. Gynec Obstet, 26: 265-69.
16. Armon, P.J., 1978. Carcinoma of the cervix in Tanzania. East Afr. Med. J., 55: 534-537.
17. Parkin, D.M., F. Bray, J. Ferlay and P. Pisani, 2005. Global Cancer Statistics, 2002. CA Cancer J. Clin., 55: 74-108.
18. Nkyekyer, K., 2000. Pattern of Gynecologic Cancers in Ghana. East Afr. Med. J., 10: 534-8.
19. Fonn, S., B. Bloch, M. Mabina, S. Carpenter, H. Cronje, C. Maise, M. Bennun, G. Du Toit, E. De Jonge, I. Manana and G. Lindeque, 2002. Prevalence of Pre-Cancerous Lesions and Cervical Cancer in South Africa-A multicenter study. South African Medi. J. 92: 148-156.
20. Duda, R.B., G.L. Chen, A.G. Hill, R. Darko, R.M.K. Adanu , J. Seffah and J.K. Anarfi, 2005. Screening for cervical cancer still not included as routine health care for women. Accepted, IJTM.
21. Davey, D.D., 2005. J. L Gen Tract Dis. Cytopathology update on atypical squamous cells, 9: 124-129.
22. Sawaya, G.F., A.D. Brown, A.E. Washington and A.M. Garber, 2001. Current Approaches to Cervical Cancer Screening. New England J. Medi., 344: 1603-1607.
23. Cannistra, S.A. and J.M. Niloff, 1996. Cancer of the uterine cervix. New England J. Med., 334: 1030-38.
24. Kim, J.J., T.C. Wright and S.J. Goldie, 2005. Cost-effectiveness of human papillomavirus DNA testing in the United kingdom, The Netherlands, France and Italy. J. Natl. Cancer Inst., 97: 888-895.
25. Rogo, K.O., J. Omany, J.N. Onyango, S.B. Ojwang and U. Stendahl, 1990. Carcinoma of the cervix in the African setting. Int. J. Gynec Obstet., 33: 249-55.