

Prevalence of cervical cancer and pre-cancerous lesions among unscreened Women in Kumasi, Ghana

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Abstract

Ghana does not have a universal population-based cervical cancer screening program and there is very limited information about the distribution of cervical epithelial cell lesions. This study provides evidence that a moderately high prevalence of cervical cancer and precancerous lesions exists among unscreened women in Kumasi.

The prevalence of cervical epithelial cell abnormalities among a cross-section of women attending cervical cancer screening for the first time in a suburb of Ghana from 2011 to 2014 was studied. Cervical smears were prepared and examined independently by 2 cytotechnologists and confirmed by a pathologist. Cervical lesions were classified according to the Bethesda System for cervical cytology 2001.

Out of the 592 women for whom a Pap smear was available for evaluation, 555 (93.8%) were negative for intraepithelial lesion or malignancy. Eight women (1.4%) showed atypical squamous cells of undetermined significance (ASCUS), 9 (1.4%) low-grade squamous intraepithelial lesions, and 2 (0.3%) high-grade squamous intraepithelial lesions. A total of 15 (2.5%) smears were unsatisfactory for cervical cytology. Additionally, 3 women (0.5%) had squamous cell carcinoma, giving an overall rate of 3.7% for epithelial cell abnormalities.

Cervical cancer and precursor epithelial cell abnormalities are common among women in Kumasi for a disease that can be prevented by early detection through routine screening and management. This study provides adequate background data to recommend the implementation of cervical cancer screening in all eligible women in Ghana.

Abbreviations: AIS = adenocarcinoma-in-situ, ART = antiretroviral therapy, ASCUS = atypical squamous cells of unknown significance, CHRPE = committee on human research, publication and ethics, CIN = cervical intraepithelial lesion, ECA = epithelial cell abnormalities, GHS = Ghana Health Service, HSIL = high-grade squamous intraepithelial lesion, KATH = Komfo Anokye Teaching Hospital, KMHD = Kumasi Metro Health Directorate, KNUST-SMS = Kwame Nkrumah University of Science and Technology, School of Medical Sciences, LSIL = low-grade squamous intraepithelial lesion, PPS = probability proportional to size, SAHS = school of allied health sciences, SCC = squamous cell carcinoma, WHO = World Health Organization, WIFA = women in fertility age.

Keywords: cervical cancer, HPV, Kumasi, precancerous lesions

1. Introduction

Cervical cancer is the second most common malignancy among women globally after breast cancer and represents 13% of female cancers in developing countries.^[1] The burden of cervical cancer in developing countries is estimated to be about 86% of the total

global burden of the disease.^[2,3] This is largely due to the absence of a well-developed national cervical cancer screening programme and health insurance cover to remove economic barriers to cervical screening.

The highest morbidity statistics are reported for sub-Saharan Africa, South America, South-Central Asia and South-Eastern Asia.^[2] In West Africa, estimated age-standardized rates per 100,000 women per year range from 26.9 in Cote D'Ivoire, through 28.6 in Burkina Faso, 30.0 in Togo, 33.0 in Nigeria, 39.5 in Ghana to 56.3 in Guinea as compared to 15.2 in the world.^[4]

Cervical cancer is the end-stage of a sequence of clinically defined lesions that occur in the cervical epithelium. The spectrum of precursor cervical squamous cell abnormalities detected microscopically begins with mild dysplasia known as low-grade squamous intraepithelial lesions (LSIL) according to the Bethesda System for reporting cervical cytology corresponding to histological cervical intraepithelial neoplasia (CIN) 1.^[5] The earliest morphologic change corresponding to this category, mild dysplasia of the epithelial lining of the cervix, is essentially undetectable by the woman. Cellular changes associated with human papillomavirus (HPV) infection, such as koilocytosis, are also commonly seen. LSIL may progress into high-grade squamous intraepithelial lesions (HSIL) characterized by moderate and severe dysplasia. This stage corresponds to histological CIN 2 and CIN 3 or carcinoma in situ.^[6] Endocervical adenocarcinoma in situ (AIS) is the term for cervical glandular

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cell dysplasia and is a recognized precursor to endocervical adenocarcinoma.^[5] Finally, further progression results in invasive cervical cancer (squamous cell carcinoma or adenocarcinoma). In principle, these squamous and glandular precursor lesions are reversible and may or may not proceed to invasive cervical cancer. However, the higher the grade of the lesion, the more likely progression to cancer becomes.^[7] Progression to invasive disease may take several years. Knowledge of this sequence of events in the development of invasive cervical cancer has been the basis of the Papanicolaou test, a longstanding screen, for CIN and invasive cervical cancer.^[7]

The burden of cervical cancer in developing countries such as Ghana is estimated to be disproportionately high largely due to the absence of well-developed national cervical cancer screening programmes. Since there is a paucity of literature on the extent of cervical epithelial cell abnormalities among the greater fraction of unscreened women in Ghana, the present study is driven by the need for data to inform health policy formulation.

2. Participants, materials, and methods

This was a multi-centre cross-sectional study to estimate the prevalence of cervical epithelial cell abnormalities among women attending cervical cancer screening in Kumasi from May 2011 to November 2014. Per the sampling protocol, on each clinic day, women presenting to the clinic were serially numbered at all sampling centers. To mitigate systematic bias, every even-numbered client reporting to each clinic was invited to participate in the study. Women 20 years and older, who had never had a Pap smear, were eligible for inclusion. Pregnant women and non-consenting women were excluded to fulfil requirements of the institutional review committee. A few women who had undergone hysterectomy or a history of a Pap smear were excluded from the study as well. Over the course of the study, a representative sample of 600 women presenting for screening at the Cervicare Clinics of 3 major health centres in Kumasi were selected for cervical cytology. Out of this number, Pap smear results were available for only 592 eligible women. Sample size was calculated by StatCalc application of EpiInfo 7.1.2.0 (CDC, Atlanta, GA): based on an expected prevalence of 7.6%,^[8] 5% error margin and 99% confidence level, it was estimated that a sample of 600 women would provide reasonably precise sample statistics.^[9] Furthermore, since health services in the metropolis are officially organised around 5 sub-metropolitan hospitals, women invited to attend the special cervical screening program at 3 purposively chosen hospitals in the metropolis were recruited using a probability-proportional-to-size (PPS) sampling technique (Table 1).

3. Cervicare centers

The 3 selected health facilities namely Kumasi South Regional Hospital, Tafo-Government Hospital and Suntreso Hospital

Table 1
Table showing population sizes and sample size distribution (N=600).

Cervicare center	Average annual OPD attendance*	Proportionate sample (n)
Kumasi South Hospital	159,307	185
Tafo Hospital	144,824	168
Suntreso Hospital	212,177	247

* The average annual attendance is calculated from figures for 2010, 2011, and 2012 calendar years.
Source: KMH, 2013.

together serve 65.8% of the total Kumasi population and 70.5% of the total population of women of fertility age (WIFA) in Kumasi. Located in the Asokwa sub-metro, the Kumasi South Regional Hospital (KSRH), 1 of 3 Cervicare clinics in the Region serves the people of Asokwa, Ahensan, Atonsu, Esreso, Gyenyase and Kaase^[10] and provides healthcare services to 56 communities with approximately 650,372 residents.^[10] The Tafo Government Hospital is located at Tafo in the Manhyia North Sub-Metropolis. The Hospital serves as one of the major health facilities for people living in the northern part of the Kumasi metropolis and beyond and has a catchment size of approximately 343,431 residents in the Manhyia North area.^[10] The Suntreso Government Hospital, located at the North-Suntreso area in Kumasi provides primary healthcare to residents of the Bantama sub-metropolitan area and its environs. The Suntreso Government Hospital is located at North Suntreso and serves North and South Suntreso, Patasi, Kwadaso, Adoato, Asuoyebo, Breaman, and Suame with approximately 519,439 residents.^[10] As much as possible, the study was located in existing facilities of the Ghana Health Service's Cervicare program. Women in the target population were strategically informed, using various methods such as educational campaigns broadcast on radio and in market places, of the study and encouraged to attend for a Pap smear.

4. Cervical cytology

To ensure that the best specimens were collected for analysis, standard procedure for collecting cervical sample was followed. Papanicolaou (Pap) smear test was performed on all the women. The smears were immediately fixed with a mixture of 95% ethanol and 5% polyethylene glycol (carbowax) spray fixative (BD Diagnostics-TriPath, Burlington, NC) and sent to the Cytology Laboratory. All fixed smears arriving in the lab were left in 95% ethanol overnight to remove the carbowax protective layer and primed by hydrating in running tap water for 4 minutes. Slides were stained by the Papanicolaou technique according to standard procedure. After slides were sufficiently dried, they were cleared in xylene, and cover-slipped using DPX mountant (GCC Diagnostics, Gainland Chemical Co., Sandycroft Flints, UK). Slides were then allowed to dry on bench and then screened for presence or absence of cervical abnormalities according to the Bethesda classification.^[11]

5. Statistical analysis

Data was captured into and analysed with SPSS v.20 software (IBM Corp, Armonk, NY) and Minitab v.14 (Minitab Inc., State College, PA). For categorical outcomes, proportions are reported (with 95% confidence interval in parenthesis). For continuous variables, data is given as mean (with 95% confidence interval in parenthesis). Hypotheses comparing prevalence estimates between studies were evaluated by comparing reported proportions in Minitab. The null hypothesis was rejected for P values $< .05$.

6. Ethical issues

The study was approved by the Committee on Human Research, Publication and Ethics (CHRPE 42/11), Kwame Nkrumah University of Science and Technology, School of Medical Sciences (KNUST-SMS) and Komfo Anokye Teaching Hospital (KATH), Kumasi, the Ghana Health Service (GHS) through the Kumasi Metropolitan Health Directorate and the Protocol and

Ethics Review Committee of the School of Allied Health Sciences (SAHS), University of Ghana, Korle-Bu, Accra.

7. Results

Pap smears were obtained from 600 women from age 20 to 93 years. Four slides were lost in transport and another 4 were excluded from the study because of improper labelling, leaving a total of 592 slides for analysis. The mean age of the participants was 42.3 years (95% CI: 41.4–43.2) and median age 42 years.

Table 2 shows the demographic characteristics of the study population including the age profile. Percentages were calculated based on the total number of respondents to each demographic parameter. The 4 major ethnic groupings in Ghana were represented in the study as follows: Akan (82.7%), Mole-Dagbani (10.4%), Ewe (3.5%) and Ga-Adangbe (2.6%). Illiteracy was reported by 12.4% of the women in study. At the time of the study, 2.9% of women were still in various stages of formal school education. However, the greater fraction of the population had completed middle school/junior high school (44.0%) while 17.2% had accessed tertiary level education. More than half of women were married (57.6%) with single women accounting for 12.8% of the study participants. Regarding employment/working status, 12.3% of women were unemployed while the rest were mostly traders (42.3%) or in some other self-employment (14.6%), public sector employees (11.5%) and

Table 2
Socio-demographic characteristics of women screened for cervical cancer.

Characteristic	N (%)	%*	95% CI
Age (N=574)			
≤40	268 (46.7)	3.0	0.9–5.0
>40	306 (53.3)	8.5	5.4–11.6
Education (N=541)			
never attended	67 (12.4)	6.0	1.7–14.6
primary	73 (13.5)	4.1	0.9–11.5
middle/JHS	238 (44.0)	5.9	2.9–8.9
SHS	46 (8.5)	6.5	1.4–17.9
technical_vocational	24 (4.4)	0.0	–
tertiary	93 (17.2)	8.6	2.9–14.3
Marital status (N=554)			
single	71 (12.8)	5.6	1.6–13.8
divorced/widowed	106 (19.1)	6.6	1.9–11.3
married	319 (57.6)	6.3	3.6–8.9
cohabiting	58 (10.5)	3.4	0.4–11.9
Ethnicity (N=534)			
Akan	445 (82.7)	6.3	4.0–8.5
Mole-Dagbani	56 (10.4)	3.6	0.4–12.3
Ewe	19 (3.5)	5.3	0.1–26.0
Ga	14 (2.6)	0.0	–
Employment (582)			
unemployed	72 (12.3)	8.1	0.9–11.7
homemaker	4 (0.7)	0.0	–
private sector	33 (5.7)	0.0	–
public servant	67 (11.5)	7.5	2.5–16.6
Self employed	85 (14.6)	3.5	0.7–10.0
National service	2 (0.3)	0.0	–
Subsistence farming	14 (2.4)	7.1	0.2–33.9
trader	246 (42.3)	8.1	4.7–11.5
student	17 (2.9)	0.0	–
retired	9 (1.5)	11.1	0.3–48.2

* Row percentages computed to show within-group prevalence for cervical dysplasia. JHS= junior high school, SHS= senior high school.

private sector employees (5.7%). Table 3 details the reproductive characteristics of the population. It has been established that a woman’s reproductive characteristics may have a direct bearing on the presence of cervical abnormalities.

Out of the 592 women for whom a Pap smear was available for evaluation, 555 (93.8%) were negative for intraepithelial lesion or malignancy (Table 4). Of the women who had an abnormal cytology result, 8 (1.4%) showed atypical squamous cells of undetermined significance (ASCUS), 9 (1.5%) had low-grade squamous intraepithelial lesions, and 2 (0.3%) had high-grade squamous intraepithelial lesions. Additionally, 3 (0.5%) had cytologic features suggestive of squamous cell carcinoma giving a total of 3.7% squamous epithelial cell abnormalities. None of the women was found to have atypical glandular cells or adenocarcinoma. Forty-three women had non-specific cervicitis

Table 3
Reproductive characteristics of women screened for cervical cancer.

	N	%*	95% CI
Gravidity (N=540)			
0	35 (6.5)	2.9	0.1–14.9
1–2	102 (18.9)	5.9	2.2–12.4
3–4	160 (29.6)	3.8	0.8–6.7
≥5	243 (45.0)	8.2	5.1–12.4
Parity (N=539)			
0	70 (13.0)	1.4	0.0–7.7
1–2	177 (32.8)	7.3	3.5–11.2
3–4	186 (34.5)	7.0	3.3–10.7
≥5	106 (19.7)	5.7	1.3–10.1
Abortion (N=538)			
0	141 (26.2)	1.4	0.2–5.0
1	141 (26.2)	5.7	1.9–9.5
≥2	256 (47.6)	8.6	5.2–12.0
Age at first pregnancy (years) (N=464)			
≤17	79 (17.0)	10.1	3.5–16.8
18–21	191 (41.2)	6.8	3.2–10.4
22–25	115 (24.8)	5.2	1.2–9.3
>25	79 (17.0)	3.8	0.8–10.7
Age at coitache (years) (N=451)			
≤15	50 (11.1)	12.0	3.0–21.0
16–18	187 (41.5)	5.9	2.5–9.3
19–21	144 (31.9)	4.2	0.9–7.4
≥22	70 (15.5)	4.3	0.9–12.0

* Row percentages computed to show within-group prevalence for cervical dysplasia.

Table 4
Prevalence of cervical abnormalities among women cytologically screened in Kumasi, Ghana, 2012 to 2014.

	Cervical cytology status		
	Frequency (N)	Percentage (%)	95% CI
NILM*	555	93.8	91.8–95.7
ASCUS	8	1.4	0.4–2.3
LSIL	9	1.5	0.5–2.5
HSIL	2	0.3	0.0–1.2
SCC	3	0.5	0.1–1.5
Unsatisfactory	15	2.5	1.3–3.8
Total	592	100.0	

ASCUS=Atypical squamous cells of unknown significance, HSIL=high-grade squamous intraepithelial lesions, LSIL=Low-grade squamous intraepithelial lesions, NILM=Negative for intraepithelial lesions or malignancy, SCC=squamous cell carcinoma.

* This category also includes smears with metaplastic changes and smears without transformation zone components but no dyskaryosis seen either.

Table 5**Auxiliary cytology findings according to Pap smear results.**

Auxiliary cytology findings	Pap cytology status					Unsatisfactory	Total	95% CI
	ASCUS	HSIL	LSIL	SCC	NILM			
None	8	2	9	3	473	8	503	
Atrophic changes	0	0	0	0	16 (2.9)	2 (13.3)	18 (3.0)	1.7–4.4
BV	0	0	0	0	12 (2.2)	0	12 (2.0)	0.9–3.2
Candida	0	0	0	0	12 (2.2)	0	12 (2.0)	0.9–3.2
Candida and BV	0	0	0	0	3 (0.1)	0	3 (0.5)	0.0–1.1
Cervicitis	0	0	0	0	38 (6.8)	5 (33.3)	43 (7.3)	5.2–9.4
<i>Trichomonas vag.</i>	0	0	0	0	1 (0.0)	0	1 (0.2)	0.0–0.5
Total	8	2	9	3	555	15	592	

ASCUS = Atypical squamous cells of unknown significance, BV = Bacterial vaginosis, HSIL = high-grade squamous intraepithelial lesions, LSIL = Low-grade squamous intraepithelial lesions, NILM = Negative for intraepithelial lesions or malignancy, SCC = squamous cell carcinoma.

(7.3%), 12 had candidiasis alone (2.0%), 12 had bacterial vaginosis alone (2.0%) and 1 had *Trichomonas vaginalis* (0.2%) infection. Table 5 shows that these conditions were mainly diagnosed among cases negative for any epithelial cell abnormality.

8. Discussion

Differences in prevalence of the precancerous lesions of the uterine cervix from one population to another are mainly attributed to the existence and consistency of screening programs and management options implemented in these countries.^[2] Thus, populations with a low profile of cervical cancer prevention effort are expected to have a high burden of ECA while those with moderate level of awareness and preventive programs may also be expected to have a lower prevalence of epithelial cell abnormalities (ECA). The World Health Organisation (WHO) has published that among previously unscreened women from 25 to 65 years, the distribution of ECA are likely to be as follows: LSIL (low grade squamous intraepithelial lesion): 3% to 10%; HSIL (high grade squamous intraepithelial lesion): 1% to 5%; and invasive cervical cancer: 0.2% to 0.5%.^[12]

In this study, women in Kumasi who had never been screened for cervical abnormalities were invited to a special cervical screening program at 3 major hospitals. All levels of squamous intraepithelial lesions according to the Bethesda nomenclature were detected. The prevalence of cervical lesions of 3.7% is comparable to what has been previously reported by a smaller study with similar objective in Nkawie (3.5%) in the Ashanti Region.^[13] Relatively similar results on the prevalence of epithelial cell abnormality (ECA) have been reported in a few other resource impaired settings in sub-Saharan Africa: In a community-based study in South Africa,^[14] 2.4% of women screened were found to have low-grade squamous intra-epithelial lesions (LSIL); 1.8% had high-grade SIL (HSIL) and 0.5% had cytology results suspicious for invasive cancer. A cross-sectional study in Cameroon reported a prevalence of 3.9% for cervical precancerous lesions.^[15] In general, concordance in prevalence estimates of cervical cancer and pre-cancerous lesions can be attributed to similar healthcare budget constraints and the absence or presence of public health education programs (that increase awareness of the condition among women or promote safer sexual habits) and/or of well-coordinated cervical screening programs.

However, when compared to other studies from settings without established universal cervical screening programs in sub-Saharan Africa, the prevalence of cervical precancerous lesions

reported here is lower. In Ghana, a study among volunteer women in Agogo a district of the Ashanti Region reported an ECA prevalence of 12.5%.^[13] Thomas et al^[8] reported a prevalence of 7.6% ECA in a Nigerian population comprising atypical squamous cells of undetermined significance and atypical glandular cells 1.99%; low-grade 3.89% (LSIL) and high-grade squamous intraepithelial lesions (HSIL) 1.5%; invasive cancer 0.2% and normal 593 (53.8%) and reactive changes 427 (38.7%). More recent studies from Nigeria report even higher prevalence estimates. Data from a 5-year review of cervical cytology in Abakaliki, Nigeria has been reported by Ajah et al^[16]. The prevalence of ECA among 536 women aged 17 to 69 years was 11.2% of which 0.6% were ASC-US, 3.9% were LSIL and 6.7% were HSIL.^[16] In another study from Nigeria, the prevalence of ECA was 22.6% among 252 women aged 20 to 75 years attending clinic in a teaching hospital.^[17] Other studies from Nigeria have also reported, higher prevalence of cervical epithelial cell abnormalities.^[18,19] Studies with large sample of women from South African found higher rates of ECA than what is reported here: 15.2%^[20] and 17.3%.^[21] Additionally, similar studies from Rwanda (20%),^[22] Senegal (21.0%),^[23] Guinea (9.5%)^[24] and Gabon (13.0%)^[25] have all reported higher prevalence of precursor cervical lesions. Among a purposive sample of Ethiopian women presenting for gynecological examination, the overall prevalence of cervical epithelial cell abnormality was 14.1%; including higher diagnostic frequencies for atypical squamous cells of undetermined significance (ASCUS), low-grade SIL, high-grade SIL, and squamous cell carcinoma.^[26] Hav et al found 6.3% of women who participated in a cervical cancer screening program in Cambodia^[27] to harbor cervical epithelial cell lesions.

A major reason for disparities in study findings from this region may be the important factor of contrasting study methodology. In the present study, the moderately lower prevalence of squamous intraepithelial lesions may reflect that some effort has been made to control other sexually transmitted diseases in the population such as promotion of increased condom use for human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) prevention and may need to be investigated further.

Although this study did not check the HIV status of participants, the relationship between the prevalence of cervical lesions and that of HIV infection is well documented. Unusually high prevalence of epithelial cell abnormalities may also be an indicator for the inclusion of HIV-infected women.^[26] Immunosuppression from HIV infection is a well-known risk factor for development of precursor cervical lesions and cervical cancer.

Studies conducted in Zambia and Kenya reported higher diagnostic frequencies of cervical epithelial abnormalities among women infected with HIV.^[28,29] In Rwanda, a cross-sectional study of 293 HIV-infected women recruited at a military hospital found a 20.0% rate of ECA.^[22] In a report by Isaakidis et al,^[30] Mumbai, cervical cytology was abnormal in 19% of women recruited from an antiretroviral therapy (ART) clinic. The detection frequencies for Low-grade squamous intraepithelial lesions (LSIL) and high-grade squamous intraepithelial lesions (HSIL) were far higher than what has been reported by this study.^[30] In addition, studies in Cambodia (25.0%),^[31] the Bahamas (44.0%)^[32] and China (8.4%)^[33], among women attending HIV clinics also report an elevated prevalence of HSIL/LSIL than has been reported by this study.^[31,33]

However, prevalence of abnormal cytology is generally relatively lower in resource-endowed countries with established screening programs. Lower rates of ECA than what we found in this study have been reported among the Australian^[34] and Turkish women.^[35] Another study among Italian women also reported lesser frequencies of ASCUS, LSIL, and HSIL.^[36] Tao et al, screened a large number of women in Beijing and found that the prevalence of cervical intraepithelial neoplasia and cancer was less common than what we found in Kumasi.^[37]

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Author contributions

ETD, EKW, FAY, and RHA conceived the study, designed its protocols and prepared the final report for publication. ETD and FAY trained study nurses who performed the cervical sampling. EKW confirmed all abnormal cases and implemented quality control procedures in the cytology reporting. ETD and RHA participated in data collection, laboratory analysis and statistical analysis. All authors read and approved the final manuscript.

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