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Survey article

Cervical cancer screening at a tertiary care center in Rwanda

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ABSTRACT

In limited resource settings such as Rwanda, visual inspection with acetic acid (VIA) is the primary model for cervical cancer screening. The objective of this study was to describe clinical characteristics and outcomes for women presenting for cervical cancer screening. A prospective, observational study was conducted between September 2015 and February 2016 at Kigali University Teaching Hospital (CHUK). Women referred to the VIA clinic were enrolled and completed a semi-structured questionnaire. During the six-month study period, 150 women were enrolled and evaluated with VIA followed by colposcopy directed biopsy for VIA positive. The median age was 42 years (IQR 36–49). Only 20 (13.3%) asymptomatic women presented for screening exam, whereas 126 (84%) were symptomatic. Among symptomatic patients, more than one-third had never had a speculum exam prior to referral (n = 43). Twenty-two (14.7%) women were VIA positive, and 8 (5.3%) had lesions suspicious for cancer, while 120 (80%) were found to be VIA negative. Among women undergoing biopsy (n = 30), 11 were normal (36.7%), 5 cases showed CIN 1 (16.6%), 4 cases showed CIN 2 (13.3%), 2 cases showed CIN 3 (6.7%) and 8 were confirmed cervical cancers (26.7%). In Rwanda, VIA is the current method for cervical cancer screening. In this study, few asymptomatic patients presented for cervical cancer screening. Increasing knowledge about cervical cancer screening and expanding access are key elements to improving cervical cancer control in Rwanda.

1. Introduction

Cervical cancer is the most common cancer diagnosed among women in Rwanda (Parkin et al., 2014). The highest incidence of cervical cancer occurs in women under the age of 50. In sub-Saharan Africa (SSA), mortality from cervical cancer is a significant contributor to overall cancer-associated death for women (Torre et al., 2017). < 2% of cancer incidence and mortality data in Africa is collected via population-based cancer registry, primarily within urban setting (Ferlay et al., 2015). Despite these limitations, in 2012 there were an estimated 265,700 cervical cancer associated deaths worldwide with 60,100 of those deaths occurring in Africa (Torre et al., 2015). Cervical cancer prevention is integral to reducing cancer associated death for women in Rwanda. Cervical cancer control is possible with implementation of key strategies, including primary prevention with human papillomavirus (HPV) vaccine and national cervical cancer screening and treatment programs. Cost limitations in addition to human and health system resource shortages influence the implementation of any national cervical cancer control strategy. Only one country, South Africa, has established a national cervical cancer screening program in SSA, but with some challenges (Lim and Ojo, 2017). Cervical cancer screening rates continue to be low in SSA, ranging from 1.6% in Ethiopia to 20% in Congo; though, rural women's screening rates are often lower (Lim and Ojo, 2017). There are no population-based reports of cervical cancer screening rates in Rwanda.

Rwanda's cervical cancer control strategy includes primary prevention via school-based HPV vaccine program for girls, which in 2011 yielded three dose vaccination rate at 93.2% (Binagwaho et al., 2012). In addition, Rwanda has introduced low-cost opportunistic cervical cancer screening with visual inspection of cervix with acetic acid (VIA) and HPV-DNA test for women starting at age 35 with repeat screening at 7 years for negative results (Binagwaho et al., 2013). National programs based on cytology testing have yielded > 80% drop in

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cervical cancer incidence in high-income countries, but such a strategy continues to be difficult to implement in limited resource settings (Torre et al., 2017; Ferlay et al., 2015). In Rwanda, women undergo VIA screening at their local health center or district hospitals. The procedure is currently performed by trained nurses and primary care physicians. Women found to be VIA positive are provided cryotherapy at the time of screening, as per local standard of care. Cases suspicious for cancer are referred from primary care facilities to the referral and teaching hospitals, such as the Kigali University Teaching Hospital (CHUK). Surgical services available for treatment at CHUK include excisional procedures of the cervix and radical hysterectomy as indicated. Detection of cervical cancer at an early stage is associated with excellent survival but most women in low and middle income countries (LMICs) continue to present with advanced and often untreatable disease (Denny et al., 2017).

The present study aims to describe demographic and social factors, clinical characteristics and outcomes of patients who consult the cervical cancer screening clinic at a tertiary care setting in Rwanda. More specifically, the aim was to determine if national VIA screening centers were effectively identifying women with pre-cancer or early cancer lesions and referring them to the tertiary care center. Alternatively, if the patients were not being referred after screening, the goal was to determine what symptoms motivated women to present for cervical cancer screening services.

2. Methods

2.1. Study design and questionnaire administration

This is a prospective, observational study designed to evaluate factors associated with women presenting for cervical cancer screening to a VIA clinic at a referral hospital in Kigali, Rwanda. All women presenting for cervical cancer screening over a 6-month period from September 2015 to February 2016 were given the opportunity to participate in the study. The Research Ethics committee of CHUK and the University of Rwanda (UR) Institutional Review Board reviewed and approved this study.

A total of 150 women ultimately enrolled in the study and underwent cervical cancer screening with VIA and completed a standardized questionnaire. Women unable to read were assisted with completion of the questionnaire by study personnel. The questionnaire inquired about the following information: demographics information, clinical and behavioral health, sexual and reproductive health history including use of contraception, gynecological history, and history of cervical cancer screening, including last pap smear and prior speculum exam and length of time with presenting gynecologic symptoms.

Cervical cancer screening was performed by a physician with the assistance of one designate midwife working in colposcopy clinic. The following protocol was followed for screening: speculum examination was completed and if an obvious cancerous lesion was visible, a biopsy was obtained. For VIA positive women, a biopsy was obtained for pathology. Pathology results were communicated to patients two to four weeks following initial evaluation by telephone call. A copy of the pathology report was stored securely in the colposcopy clinic.

2.2. Statistical analysis

Data entry was completed with Epi Data 3.1. Data cleaning and error range check to enhance validity and consistency was adhered to before data analysis. Clinical and demographic variables were aggregated and summarized for the entire cohort. Location of primary residence was converted into a dichotomous variable for the purposes of statistical analysis with residence in Kigali City defined as "metro" and residence in either the Northern, Southern, Eastern, or Western provinces was defined as "non-metro". Reason for primary consult was converted into a dichotomous variable defining presenting complaint as either symptomatic (i.e., irregular bleeding, post-coital bleeding, postmenopausal bleeding, vaginal discharge, or vaginal itching/ulceration) or asymptomatic (i.e., self-referral for regular check-up). Descriptive statistics are presented as frequencies with percentages, when appropriate. Categorical variables were compared using chi-squared or Fisher's exact test, when appropriate. Continuous variables are presented as medians with interquartile range (IQR). Stata version 14.1 (StataCorp LP, College Station, TX) software was used for data management and statistical analysis. As this was a descriptive analysis no adjustment was made for multiple comparisons, and p-values < 0.05 were considered statistically significant.

3. Results

Women presenting for cervical cancer screening to the VIA clinic at CHUK were invited to participated and a total of 150 women were enrolled during a six-month study period. The median age of the patients was 42 (IQR 36–49 years). All provinces in Rwanda were represented with the majority coming from Kigali city (n = 81, 54%). Women were referred to the VIA clinic by a clinician in a district hospital 108 (72%), health center 35 (23%) and 7 (5%) other. Fortynine women (33%) reported no prior gynecologic examination with the use of a speculum to visualize the cervix. Other social demographic and clinical characteristics are detailed in Table 1.

There were some important differences that emerged when comparing symptomatic patients (n = 126, 84% of total study population) to asymptomatic patients (n = 20, 13.3%). Four patients did not respond to survey question regarding their reason for seeking consult. Among the patients who presented for asymptomatic screening exam, two were found to be VIA positive and were ultimately diagnosed with CIN 1 and CIN 2, respectively. Three-quarters of the asymptomatic population (n = 15) were from Kigali city, while the remaining 5 asymptomatic patients traveled from a non-metro location to the VIA clinic. Among the 126 women who reported symptoms, there were some important differences based on their place of primary residence (Table 2). Most patients were from Kigali City (n = 65, 51.6%) compared to a nonmetro location (n = 61, 48.4%). Most symptomatic patients reported vaginal discharge as their primary complaint (n = 96, 76.1%), however more patients from Kigali City reported pelvic pain compared to nonmetro patients (24.6% vs 1.6%, p < 0.001). Patients from Kigali City were more likely to report current use of contraception (35.4% vs. 8.2%, p < 0.001). Among symptomatic patients, more than one-third had never had a speculum exam prior to referral (n = 43).

3.1. Outcomes of VIA and follow-up biopsies

All women were screened using VIA. Among 150 patients who were screened, 22 (14.7%) were VIA positive, 8 (5.3%) patients were suspected to have cancer and 120 (80%) were VIA negative. Among the VIA negative patients, one patient underwent a biopsy showing CIN I histology. Thirty women were suspected to have either VIA positive pre-cancer lesion or cancer and underwent a colposcopy directed cervical biopsy. Histology results returned with 8 confirming cancer (26.7%), while 5 showed CIN 1 (16.6%), 4 showed CIN 2 (13.3%) and 2 showed CIN 3 (6.7%, see Table 3).

4. Discussion

Challenges and opportunities to implementation of VIA based screening have been identified in limited resource settings (Parham et al., 2015; Moon et al., 2012). In the present study, symptomatic women presented to a referral center without VIA screening performed at a lower level health facility, despite 84% of them reporting symptoms including abnormal vaginal bleeding and/or abnormal vaginal discharge. In addition, 43 (34%) women who were symptomatic had no prior speculum exam, supporting that visual inspection of

Table 1

Demographic and clinical characteristics of study participants (N = 150).

| Age, median (IQR) | 42 (36–49) |
|---|------------------------|
| Province, N (%) | |
| Kigali city (metro) | 81 (54.0) |
| Outside Kigali (non-Metro) | 69 (46.0) |
| Education, N (%) | |
| No formal education | 22 (14.7) |
| Some primary education | 64 (44.7) |
| Some secondary education | 37 (24.7) |
| Some university | 25 (16.7) |
| Occupation, N (%) | |
| Farming | 63 (42.0) |
| Civil servant | 11 (7.3) |
| Business | 32 (21.3) |
| Health worker | 13 (8.7) |
| Other | 31 (20.7) |
| Marital status, N (%) | |
| Single | 8 (5.3) |
| Married/cohabitating | 108 (72.0) |
| Divorced | 10 (6.7) |
| Widowed | 24 (16.0) |
| Age at first intercourse, N (%) | |
| 15–20 | 50 (33.3) |
| 21–25 | 64 (42.7) |
| 26–30 | 29 (19.3) |
| 31–35 | 4 (2.7) |
| 36-40 | 2 (1.3) |
| 41-45 | 1 (0.67) |
| Lifetime sexual partners, median (IQR) | 2 (1-2) |
| Gonorrhea history, N (%) | |
| Never | 137 (91.3) |
| Once | 7 (4.7) |
| > 1 time infected | 2 (1.3) |
| Unsure of history | 4 (2.7) |
| Chlamydia history, N (%) | 100 (05 0) |
| Never | 128 (85.3) |
| Once | 2 (1.3) |
| > 1 time infected | 1 (0.67) |
| Other CTD Lister | 6 (4.0) |
| Other SID history | 11 (7.3) |
| Never used (uncure | F1 (24 0) |
| Never used/ulisure | 51 (34.0) 38 (35.3) |
| Used in the next | 38 (25.3) |
| Alashal N (0/) | 61 (40.7) |
| Alcollol, N (%) | 77 (51.2) |
| Gurrent drinker | 20 (26 0) |
| Former drinker | 34 (22.7) |
| Smoking N (%) | 34 (22.7) |
| Never smoker | 128 (85.2) |
| Current smoker | 120 (00.0) 8 (5 2) |
| Former smoker | 0 (3.3) 14 (0.2) |
| Premancies median (IOR) | 5(3-7) |
| Reason for seeking consult $N (\%)^{a}$ | 3 (3-7) |
| Regular check-up | 20 (13 3) |
| Vaginal discharge | 26 (13.3) |
| Rleeding | 11 (7 2) |
| Delvic pain | 11(7.3) 17(11.2) |
| Vaginal ulceration | 2(12) |
| Timing of last speculum exam N (%) | 2 (1.3) |
| Never | 49 (32 7) |
| Weeks | 44 (29 3) |
| Months | 35 (23 3) |
| Vears | 33(23.3) 22(14.7) |
| 1000 | 22 (1 7 ./) |

^a Four patient had missing reason for consult.

the cervix with or without VIA was missing in the evaluation of gynecologic clinical exam prior to referral from an outside facility. The high VIA positive screen result (20%) in our study population reflects a more symptomatic group of patients. A similar VIA positive rate (19.6%) was reported in a study conducted in western Kenya, although 71% of the women were HIV-positive (Khozaim et al., 2014). A study conducted in Mozambique, 21% HIV-positive rate, 8% of women screened had VIA positive result (Moon et al., 2012).

Key strategies have been implemented in Rwanda to lay the ground

Table 2

Clinical characteristics of symptomatic^a patients based on geographic location.

| Variable | Kigali city (n = 65) | Non-Urban ($n = 61$) | p-value |
|-------------------------------------|-------------------------|------------------------|---------|
| Cervical cancer, N (%) ^b | 1 (1.5) | 6 (9.8) | 0.056 |
| Reason for consult, N (%) | | | < 0.001 |
| Vaginal discharge | 37 (56.9) | 59 (96.7) | |
| Bleeding | 10 (15.4) | 1 (1.6) | |
| Pelvic pain | 16 (24.6) | 1 (1.6) | |
| Vaginal ulceration | 2 (3.1) | 0 (0.0) | |
| Contraception use, N (%) | | | < 0.001 |
| Never used/unsure | 13 (20.0) | 32 (52.5) | |
| Currently using | 23 (35.4) | 5 (8.2) | |
| Used in the past | 29 (44.6) | 24 (39.3) | |
| Length of symptoms, N | | | < 0.001 |
| (%) | | | |
| Weeks | 36 (55.4) | 9 (14.8) | |
| Months | 17 (26.2) | 30 (49.2) | |
| Years | 12 (18.5) | 22 (36.1) | |
| Last speculum exam, N | | | < 0.001 |
| (%) | | | |
| Never | 29 (44.6) | 14 (23.0) | |
| Weeks | 23 (35.4) | 16 (26.2) | |
| Months | 5 (7.7) | 23 (37.7) | |
| Years | 8 (12.3) | 8 (13.1) | |
| Last pap smear, N (%) | | | 0.304 |
| < 5 years ago | 9 (18.0) | 9 (29.0) | |
| \geq 5 years ago | 1 (2.0) | 2 (6.5) | |
| Unsure | 2 (4.0) | 0 (0.0) | |
| Never | 38 (76.0) | 20 (64.5) | |

^a Symptomatic defined as patients who described primary reason for consult as bleeding (i.e., irregular, post-coital, post-menopausal), vaginal discharge/ulceration, and/or pelvic pain.

^b One patient diagnosed with cervical cancer had missing district of primary residence.

Table 3Results of final pathology for VIA positive patients.

| | N | % per total screened | % among VIA + /CA suspicious |
|--|-----|-------------------------|------------------------------|
| Total number of women who were screened | 150 | 100.0 | N/A |
| VIA positive or suspicious for | 30 | 20.0 | 100.0 |
| cancer | | | |
| Normal | 11 | 7.3 | 36.7 |
| CIN 1 | 5 | 3.3 | 16.6 |
| CIN 2 | 4 | 2.7 | 13.3 |
| CIN 3 | 2 | 1.3 | 6.7 |
| Cervical cancer | 8 | 5.3 | 26.7 |

CIN = cervical intraepithelial neoplasia; VIA: visual inspection with acetic acid.

work for optimal cervical cancer control. Coverage of basic health services within the community-based health insurance program in Rwanda (Mutuelle de Santé) provides coverage for 90% of the population, and with additional private health insurance coverage, < 4% of the population is uninsured (Nyandekwe et al., 2014). Multi-level health systems, from community health centers to district hospitals and referral centers, exist to provide scaled-up level of medical services in Rwanda. These basic healthcare provisions include maternal and child health services, preventative health services, such as breast clinical exam and VIA exam for cervical cancer screening (Binagwaho et al., 2013; Bucagu et al., 2012). Non-financial barriers to accessing health care can exist that reduce uptake of cancer screening services. In this study, current contraceptive usage was significantly higher among women referred from the urban region of Kigali versus outlying regions, likely reflecting increased health care utilization in urban areas.

Patient-related barriers have been identified in sub-Saharan Africa, including lack of cervical cancer knowledge and lack of awareness of available services (Lim and Ojo, 2017; Fort et al., 2011). VIA screening has been available in Rwanda at sporadic private and public health

facilities since at least 2010. In December 2012, an intensive national training of nurses and doctors in VIA occurred as part of the implementation of the national strategic plan for cervical cancer prevention, care and control (Binagwaho et al., 2013). Limited data exist as to the quality control and continued performance of VIA centers in Rwanda. In this study, 20% of women had VIA positive result or suspicious for cancer clinical finding.

Challenges to scale-up of VIA based programs have been identified among other SSA countries. In Kenya, implementation of a VIA program noted loss of follow-up and lack of appropriate pathology services as program challenges (Khozaim et al., 2014). In Zambia, a multifaceted approach was utilized with success to scale-up of VIA screening: challenges addressed include shortage of trained nurses and physicians. shortage of cryotherapy supplies and inefficient management of the program (Parham et al., 2015). The need for multiple rounds of VIA screening for optimal program performance when accounting for increased human and health system resources supports consideration of alternative models for cervical cancer screening in limited resource setting. HPV-DNA testing has higher sensitivity and specificity and, when coupled with self-testing, may prove to be a more cost-effective model in resource-constrained settings (Fitzmaurice et al., 2015). More importantly, outside of cervical cancer screening programs, women presenting with cervical cancer-related symptoms to health facilities must be appropriately evaluated by trained health personnel with speculum examination to optimize early diagnosis of cervical cancer.

As this study was conducted within a referral center in an urban city of Rwanda, the patient population and their health behavior characteristics may not reflect the rural regions or general population of Rwanda. Data on HIV co-infection was not available, although this is a known and significant factor in cervical cancer disease in SSA. Furthermore, even though Rwanda instituted a national vaccination program that include the HPV vaccine in 2011, this vaccine program was targeted at primary school age girls and our study group is likely reflective of nonvaccinated population. These limitations may be addressed in future, prospective studies that seek to improve rates of cervical cancer screening and early detection in resource-limited settings.

5. Conclusion

In Rwanda, VIA is the current method for cervical cancer screening with VIA services to be provided at community health centers, district hospitals and referral centers. In this study, few asymptomatic patients presented for screening services available at CHUK. Of those women who presented for screening and were biopsied, 26% were diagnosed with cervical cancer. Increasing knowledge about cervical cancer screening and expanding access are key elements to improving cervical cancer control in Rwanda. Additional studies are warranted to assess uptake of current cervical cancer screening with VIA in Rwanda.

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Conflicts of interest

The authors report no conflicts of interest.

References

- Binagwaho, A., Wagner, C.M., Gatera, M., Karema, C., Nutt, C.T., Ngabo, F., 2012. Achieving high coverage in Rwanda's national human papillomavirus vaccination programme. Bull. World Health Organ. 90 (8), 623–628.
- Binagwaho, A., Ngabo, F., Wagner, C.M., Mugeni, C., Gatera, M., Nutt, C.T., et al., 2013. Integration of comprehensive women's health programmes into health systems: cervical cancer prevention, care and control in Rwanda. Bull. World Health Organ. 91 (9), 697–703.
- Bucagu, M., Kagubare, J.M., Basinga, P., Ngabo, F., Timmons, B.K., Lee, A.C., 2012. Impact of health systems strengthening on coverage of maternal health services in Rwanda. 2000–2010: a systematic review. Reprod. Health Matters 20 (39), 50–61.
- Denny, L., de Sanjose, S., Mutebi, M., Anderson, B.O., Kim, J., Jeronimo, J., et al., 2017. Interventions to close the divide for women with breast and cervical cancer between low-income and middle-income countries and high-income countries. Lancet 389 (10071), 861–870.
- Ferlay, J., Soerjomataram, I., Dikshit, R., Eser, S., Mathers, C., Rebelo, M., et al., 2015. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. Int. J. Cancer 136 (5), E359–E386.
- Fitzmaurice, C., Dicker, D., Pain, A., Hamavid, H., Moradi-Lakeh, M., MacIntyre, M.F., et al., 2015. The global burden of cancer 2013. JAMA Oncol. 1 (4), 505–527.
- Fort, V.K., Makin, M.S., Siegler, A.J., Ault, K., Rochat, R., 2011. Barriers to cervical cancer screening in Mulanje, Malawi: a qualitative study. Patient Prefer. Adherence 5, 125–131.
- Khozaim, K., Orang'o, E., Christoffersen-Deb, A., Itsura, P., Oguda, J., Muliro, H., et al., 2014. Successes and challenges of establishing a cervical cancer screening and treatment program in western Kenya. Int. J. Gynaecol. Obstet. 124 (1), 12–18.
- Lim, J.N., Ojo, A.A., et al., 2017. Eur. J. Cancer Care (Engl.) 26 (1).Moon, T.D., Silva-Matos, C., Cordoso, A., Baptista, A.J., Sidat, M., Vermund, S.H., 2012.Implementation of cervical cancer screening using visual inspection with acetic acid
- in rural Mozambique: successes and challenges using HIV care and treatment programme investments in Zambezia Province. J. Int. AIDS Soc. 15 (2), 17406.
- Nyandekwe, M., Nzayirambaho, M., Baptiste, Kakoma J., 2014. Universal health coverage in Rwanda: dream or reality. Pan. Afr. Med. J. 17, 232.
- Parham, G.P., Mwanahamuntu, M.H., Kapambwe, S., Muwonge, R., Bateman, A.C., Blevins, M., et al., 2015. Population-level scale-up of cervical cancer prevention services in a low-resource setting: development, implementation, and evaluation of the cervical cancer prevention program in Zambia. PLoS One 10 (4), e0122169.
- Parkin, D.M., Bray, F., Ferlay, J., Jemal, A., 2014. Cancer in Africa 2012. Cancer Epidemiol. Biomark. Prev. 23 (6), 953–966.
- Torre, L.A., Bray, F., Siegel, R.L., Ferlay, J., Lortet-Tieulent, J., Jemal, A., 2015. Global cancer statistics, 2012. CA Cancer J. Clin. 65 (2), 87–108.
- Torre, L.A., Islami, F., Siegel, R.L., Ward, E.M., Jemal, A., 2017. Global cancer in women: burden and trends. Cancer Epidemiol. Biomark. Prev.