

Cervical cancer screening and practice in low resource countries: Nigeria as a case study

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ABSTRACT

Cervical cancer is the most common female genital tract malignancy in Nigeria and majority of the patients present with advanced disease. It is a preventable cancer as there are well-defined treatable premalignant phases. The objective of the study is to review the burden of cervical cancer, its screening modalities, and practice of screening and treatment in low resource countries with emphasis on Nigeria. This is a review involving internet and literature search. While developed countries have recorded significant reduction in the incidence of cervical cancer owing to organized screening programs, treatment of premalignant cervical lesions, and follow-up of treated cases, developing countries including Nigeria are yet to optimally utilize screening services due to lack of organized population-based screening programs with only pockets of screening services which are at best opportunistic. This has not reduced the incidence of cancer because only a fraction of the target population is covered. Apart from this, loss to follow-up is rampant. The level of awareness of cervical cancer and its preventive strategies are low among the population and policymakers in Nigeria. There is no organized screening program, and the few services available are only opportunistic with little or no impact. Development of cervical cancer screening policy and institution of organized screening program targeted at covering $\geq 80\%$ of population at risk is fundamental. There is also a need for widespread education of the populace on the burden of cervical cancer and the public health importance of the disease using the mass media, counseling at antenatal clinics, and the involvement of men will contribute immensely to reduction in the incidence of cervical cancer. Decentralization of services by incorporation of cervical screening and treatment in primary health care programs will ensure adequate rural-urban coverage.


Key words: Cervical cancer screening; human papillomavirus, low resource countries; Nigeria; premalignant disease.

Introduction

Cervical cancer is the second most common cancer in women globally after breast cancer.^[1] It is a major public health challenge globally and the most common malignancy of the female genital tract in Nigeria. It is a preventable cancer as it has a well-defined premalignant phase where treatment could be offered before invasive cancer develops. This approach has led to a significant decline in the incidence of cervical cancer in developed countries.

Screening helps to identify women with premalignant lesions, and treatment or follow-up could be offered as appropriate. Screening could also afford the detection of early stages of invasive cancer where institution of treatment promises favorable prognosis.^[2] The ease with which the cervix can be

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accessed or inspected visually by speculum examination and sample obtained for analysis makes cervical cancer screening highly feasible and practicable in clinic setting.

Epidemiology

An estimated 528,000 new cases of cervical cancer were diagnosed in 2012 with 266,000 deaths globally.^[3] About 90% of these deaths occur in low- to middle-income countries, and if current trends persist, it was estimated that about 25% rise in the deaths may be recorded in the following 10 years.^[4] Cervical cancer has a global distribution but varying incidence and prevalence with different geographical locations as a result of unequal availability and practice of screening for the premalignant disease.^[3] Deaths from cervical cancer occur in the prime of lives when women are contributing immensely to the socioeconomic lives of the family and communities.

While the global average incidence of cervical cancer is 15.2/100,000 women, the Sub-Saharan Africa has an incidence of 19.1.^[5] Reports from regional population-based cancer registries in Nigeria revealed age-specific rate of 36.0, 30.3, and 21.0/100,000 women for Ibadan, Abuja, and Calabar cancer registries, respectively, and mean age at diagnosis of cervical cancer being 56.1, 52.3, and 50.1 years accordingly.^[6,7] Occurrence of cervical cancer at lower ages is notable in the reports from these registries. This could be attributed to earlier age at sexual debut, lifestyle changes such as smoking and multiple sexual partners.

Due to gross underreporting of cancers in Nigeria, these reports may demonstrate the iceberg phenomenon. A community-based prevalence study by Thomas *et al.* in Ibadan Southwest Nigeria found a prevalence of 7.6% for cervical epithelial abnormalities (both premalignant and malignant lesions).^[8]

Nigeria is the most populous African country. While about 92,000 new cases of cervical cancer were recorded by the African regional office of the World Health Organization (WHO) and 57,000 deaths, Nigeria had about 10,000 new cases and 8,000 mortalities in the same period.^[4]

Etiopathogenesis

Persistent high-risk human papillomavirus (hrHPV) infection of the cervix is considered the main etiological factor in over 99% of cervical cancer. While HPV transmission is predominantly sexual, 90% of immunocompetent women will have a spontaneous resolution over a 2-year period.^[9] Out of about 200 HPV genotypes known, over 40 types infect the genital tract out of which 15 are known to be oncogenic

to humans.^[10] The two most common hrHPV types are the HPV-16 found in 50%–70% of cervical cancers and HPV-18 found in 7%–20%.^[9]

Other hrHPV genotypes include HPV-31, 33, 35, 45, 52, and 58. HPV genotypes that are less frequently found in cervical cancer include HPV-39, 51, 56, and 59. Furthermore, HPV-68 was termed “probably carcinogenic to humans.” Low-risk HPV genotypes are associated with benign lesions of the cervix including viral warts. They are HPV-6, 11, 42, 43, 44, 54, and 55.^[9]

A cross-sectional study of HPV distribution in invasive cancer of the cervix in Sub-Saharan Africa found 90.4% of the cancers to be HPV positive with the most detected HPV genotypes being HPV-16 (50.7%), HPV-18 (19.2%), HPV-45 (10.1%), HPV-35 (9.7%), HPV-33 (5.0%), and HPV-52 (4.5%).^[11]

The pattern of the age-specific prevalence of oncogenic HPV varies widely. In general, the prevalence is highest in the twenties and usually lower at older age. Majority of HPV infections acquired at this age are cleared by the immune system of the affected women; clearance becomes more difficult with age. In some countries, a second small peak in prevalence is seen in women 45–50 years, and in others, the prevalence is very low in all ages.^[12,13] Strangely, in southern Nigeria, the prevalence of oncogenic HPV is high across all ages with slight peaks in women of 15–29 and 60–69 years.^[14,15]

Most of the predisposing factors for cervical cancer either increase the likelihood of HPV infection or encourage its persistence. Epidemiologic risk factors for cervical cancer include multiple sexual partners, early age at sexual debut, high risk sexual partner, immunosuppression from HIV infection or other causes and long-term oral contraceptive use.^[9] These major risk factors have been shown to be prevalent in Nigeria.

Continuous metaplastic changes in the dynamic transformation zone predispose to HPV infection, and the persistence of the infection may ultimately lead to malignant transformation. The squamocolumnar junction (SCJ) of the cervix is also dynamic as it varies in location throughout the reproductive ages, extending outward at puberty, and by physiological changes, the columnar epithelium is transformed to squamous epithelium as it becomes exposed to the acidic environment of the vagina. This cycle is repeated following conditions that raise estrogen levels and lead to extensive growth of the columnar epithelium toward the ectocervix, such as pregnancy and use of oral

contraceptive pills. The transformation zone, region of the cervix between the old and new SCJ, is the site where HPV infection and persistence could develop into premalignant and malignant lesions as integration of the viral DNA into the basal cells of the epithelium results in immortalization and rapid turnover of the basal cells. At this phase, awareness and knowledge of cervical cancer coupled with good health-seeking behavior make a woman to get screened and benefit from appropriate treatment thus preventing the occurrence of invasive cancer.

Before the occurrence of invasive cervical cancer, the premalignant lesions histologically described as cervical intraepithelial neoplasia (CIN) are classified as CIN I, II, or III with decreasing tendency to spontaneous regression. Identification of women at these stages through screening affords the opportunity of follow-up or treatment and thus reduction in the prevalence of cervical cancer if well implemented.^[9,10]

Components of Cervical Cancer Prevention and Control

A complete cervical cancer prevention model includes three interdependent components: primary, secondary, and tertiary prevention. While HPV vaccination and health education form the basis of primary prevention, screening and treatment of premalignant cervical lesions constitute the secondary prevention modalities while tertiary prevention entails the management of invasive cervical cancer using surgery, radiotherapy, chemotherapy, or palliative care as appropriate.^[11]

Screening modalities

CIN is the premalignant lesion of the cervix. In the words of Sir John Williams in 1886, "It presented no distinct symptoms, and was discovered accidentally." Prevention strategies for cervical cancer have gone through series of revolutionary changes. The goal of screening and treating cervical premalignant lesion is to decrease the incidence of cervical cancer and the associated mortality by truncating the progress from precancerous lesion to invasive cancer.

The United States Preventive Services Task Force and the joint partnership of American Cancer Society, American Society for Colposcopy and Cervical Pathology, and American Society for Clinical Pathology (ACS/ASCCP/ASCP) recommended 3-yearly cervical cytology screening for women aged 21–29 years while those above 30 years should have cytology and HPV cotesting every 5 years or cytology alone every 3 years. Screening should be stopped at 65 years of age provided the results in the preceding 10 years were negative.^[16]

Cytology-based screening requires obtaining exfoliated epithelial cells of the transformation zone and fixing on a slide (conventional Pap smear) or put in a transport medium (liquid-based cytology) for cytological analysis under a microscope. Advantages of conventional cytology include its proven effectiveness, wide acceptability in high-income countries, and well-established quality control measures. It is however difficult to introduce or maintain and requires clinical and laboratory quality assurance. It requires transportation from clinic back to the laboratory and multiple patient visits.^[11] The liquid-based cytology additionally allows molecular testing from the sample collected but its laboratory requirements are more expensive than for conventional cytology. The sensitivity of Pap smear ranges from 20% to 52% and specificity from 90% to 95%.^[17] Any abnormality found is classified using the Bethesda system (TBS), and appropriate follow-up or intervention is instituted.

TBS was designed to enhance communication between the laboratory and the clinician while providing reproducible data for global comparison. Since its inception in 1988, it has evolved to accommodate the improvement in technology as regards cervical cancer screening and prevention. The third update released in 2014 included an online version for educational purpose and also birthed the Bethesda Interobserver Reproducibility Study-2 (BIRST-2). TBS-2014 takes into account the specimen type, adequacy of sample, result of test/interpretation, and any adjunctive testing.^[18]

Visual screening methods include visual inspection with acetic acid (VIA) or with Lugol's iodine to detect characteristic changes in the presence of precancerous lesions. Visual screening test is simple, inexpensive and requires brief training and minimal infrastructure. The results are available immediately, and treatment can be offered simultaneously. This has been described as the see-and-treat approach. It is prone to interobserver variation, there is the need for supervision, and the nonapplicability in postmenopausal women in whom the transformation zone is frequently within the endocervical canal are some of its setbacks.^[1,9]

HPV DNA testing is incorporated into prevention programs in high resource settings as a primary screening test. The possibility of self-collection by the woman simply by inserting the small collecting brush deep into the vagina may make it more acceptable. Reflex HPV testing prevents overtreatment in women with abnormal Pap smear and normal colposcopic studies with negative hrHPV testing.^[19] In the light of present-day understanding of the molecular mechanism of cervical cancer, detection of HPV E6 and E7 mRNA in liquid-based cervical cytology specimens has shown higher sensitivity and specificity for hrHPV screening.^[20]

Colposcopy is used in the evaluation of an abnormal cervical smear with the aid of illuminated low-power magnification (5–15×). Abnormalities such as vascular pattern, border characteristics, surface pattern, and area of lesion are better appreciated with a colposcope.^[9,21] While colposcopy allows directed biopsy of abnormal area on the cervix, it is resource intensive, requires training and pathology services. Endocervical curettage of inaccessible portion of the cervix provides samples for histologic evaluation.^[1]

Spectroscopic techniques have been shown to be reliable point-of-care tests in screening for cervical premalignant lesions. Working on the principle of fluorescence and reflectance spectroscopy, it has the potential of quantitatively assessing cellular and tissue changes. Awolude *et al.* reported a sensitivity of 92.3% for multimodal hyperspectroscopy among 100 previously screened women and significant reduction in the number of unwarranted colposcopy and cervical biopsy.^[22] Spectroscopic finding of hr result was found to correlate with the histological diagnosis of cervical dysplasia in a study in Ekiti state, south-western Nigeria, thereby further supporting its usefulness in cervical cancer screening.^[23]

The WHO recommends commencement of cervical cancer screening as a form of secondary prevention from the age of 25 years. The United States Center for Disease Control recommends screening between ages of 21 and 65 years. Several regional guidelines are also available with respect to human and material resources at the disposal of the region.^[24] The screen-and-treat approach is recommended for low resource settings, screening being with modalities such as VIA while treatment could be offered with cryotherapy or loop electro-surgical excision procedure.^[25]

The Nigeria Experience

In contrast with the developed countries where optimal practice of screening services has led to significant reduction in incidence and prevalence of cervical cancer, little improvement has been recorded in most developing countries. Gaffikin *et al.* reported that lack of a comprehensive national screening program in Ghana coupled with low rate of patronage of cervical cancer screening services hamper its prevention in the country.^[26] Lack of awareness and knowledge of cervical cancer further reduces uptake at the few centers where screening facilities are available.^[27]

Lack of comprehensive policy for cervical cancer prevention and inadequate publicity of available strategies culminate in low practice of prevention modalities in many developing countries. Inaccessible screening facilities and high financial

cost have been highlighted as impediments to utilization of such services.

About 40 million women are at risk of developing cervical cancer in Nigeria, with a national age-standardized incidence rate of 33.0 cases per 100,000 women per year.^[28,29] The country lacks a well-implemented national cervical cancer policy, and late presentation of cervical cancer in majority of patients is common.^[30,31] The situation is made worse by the fact that most health facilities lack appropriate infrastructure for effective management of the advanced disease.^[30,31] Where they are available, the screening centers are inadequate in number to cater for the populace and such centers are mostly found in the urban settlements while the highly populated rural communities are underserved. Whereas primary health centers which are found in nearly every community are not equipped to provide these services. With the absence of organized screening policy, the screening offered to women occurs at the request of patients, suggestion of health personnel, or through awareness programs organized by individuals or nongovernmental organizations. Some of the screening programs are episodic, often concentrated around the period of cervical cancer prevention week or occasional infrequent free health services organized by politicians, philanthropists, and citizens in diaspora rather than being available all-round the year.^[32] Screening services are also available at some secondary and tertiary health facilities either by state or institutional initiatives, and in these places, services are prostrate and epileptic for lack of human resources and basic materials.^[33] The available data on cervical cancer screening in Nigeria are majorly hospital based and may not be representative of the populace.

There is low level of awareness of the burden of cervical cancer, its predisposing factors, prevention strategies, and centers where such services could be offered. Some studies among female university undergraduates across the country corroborated this.^[34,35] In places where the level of awareness is high, uptake of screening is expected to be commensurate.

Despite the use of conventional Pap smear in some facilities in the country, no significant improvement in the incidence of cervical cancer has been reported. This may not be unconnected to the multiple patient visits required by this method along with its personnel requirement; the asymptomatic patient is thus easily lost to follow-up. This has led to the adoption of screen-and-treat approach recommended by the WHO using VIA while referring women that require treatment to the appropriate centers. Poor specificity and reproducibility may however challenge the use of VIA.^[36,37] Importantly too, screening has not made much

impact because only a small fraction of the population at risk are screened. Local studies have shown that only very few women have had more than one Pap smear.^[38]

In the year 2001, the National Reproductive Health Policy and Strategy aimed at achieving quality reproductive and sexual health for all Nigerians was developed as a follow-up of the International Conference on Population and Development held in Cairo in 1994. Cervical cancer control was captioned under “other reproductive health conditions” with a target to promote screening programs for early detection of cervical, breast, and prostatic cancer. National statistics in measuring the outcome of this plan is lacking. However, institutional data and those from regional cancer registries revealed no significant improvement in the trend. Furthermore, the strategic health development plan of the federal government for 2010–2015 did not specify the modalities for the control of cervical cancer.^[39]

Factors such as other competing health needs (Malaria, HIV/AIDS, etc.), poor political will, low budgetary allocation to health, and inadequate health service delivery system may be contributory to the poor progress made in cervical cancer control.

Facing the future

The statistics relating to cervical cancer in Nigeria is worrisome, and if significant improvements are to be recorded in the future, efforts must be made to scale-up screening services in every part of the country. This could best be achieved by a comprehensive national cervical cancer screening program that targets to cover $\geq 80\%$ of the population at risk.

Education of the populace and health-care providers on cervical cancer, its risk factors, and preventive strategies is fundamental in the control of the disease. This will go a long way in increasing the uptake of screening and adherence to recommendations of treatment where applicable.^[40] Integration of single visit screen and treat strategy in the routine services of primary health centers in Nigeria will ensure that underserved populations are reached. This will ensure decentralization of services and optimal rural-urban coverage.^[33]

The role of men is vital in promoting the uptake of screening services. Awareness and advocacy measures should not exclude them if many gains are to be recorded. A large proportion of women have contact with the health facilities only in pregnancy. Thus, antenatal care education should incorporate cervical cancer awareness and screening promotion.^[41]

Multimedia health education and mass media campaigns are veritable tools to improve uptake of cervical cancer screening services. They could be employed to create awareness and address pertinent issues and women’s fears concerning screening programs.^[41,42] Remote communities lacking in basic infrastructures such as electricity could benefit from the use of handheld mobile colposcopes for screening and cryotherapy for treatment.

HPV vaccines are in use and offer primary prevention against cervical cancer. While available vaccines target mostly HPV 16 and 18 which account for majority of cervical cancer cases worldwide, cross-protection against other oncogenic HPV subtypes is well known. In a study titled “Modeling Optimal Cervical Cancer Prevention Strategies in Nigeria,” Demarteau, Morhason-Bello, Akinwunmi, and Adewole found that in a low resource economy like Nigeria, an appropriate combination of vaccination and screening will ensure efficient use of limited resources.^[43] Unlike most low resource countries where GAVI has introduced free HPV vaccine as part of routine immunization, Nigeria has not been listed for this benefit because of our inability to deliver the routine immunization.^[44]

Conclusion

Despite the feasibility of cervical cancer eradication through screening and treatment of premalignant lesions, the statistics in the developing countries is appalling. Barriers to effective screening range from low level of awareness of the disease in the generality of the populace including the literate to lack of organized screening policy and poor rural-urban coverage. There is a need to intensify global prevention through advocacy, education, information, and carriage of preventive programs to reach every woman including rural community dwellers by integration of cervical cancer screening into primary health-care services in the country.

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Conflicts of interest

There are no conflicts of interest.

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