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Disparity in the incidence, prevalence, etiology, screening and presentation of cervical cancer between Africa and America

Abstract

Cervical cancer represents a huge burden of non-infectious disease globally. It is the fourth most common cancer in women and accounts for over half a million deaths every year. In low and middle income countries (LMIC) it is the second most common cancer among women closely following breast cancer. The aetiological agent implicated in this disease is the human Papillomavirus. The high-risk human papilloma virus (HPV) has been mostly implicated. Worldwide, the most common high-risk human papillomavirus implicated in cervical cancer are type 16 and 18. The viral infection of the uterine cervical epithelium initially causes the development of precancerous lesions referred to as cervical intraepithelial lesions/squamous intraepithelial lesions which could take many years to progress into cancer. The Papanicoulao smear test done for the screening of precancerous cervical lesions has been known to be effective in preventing the disease. The commonest types of cervical cancer are the cervical squamous cell carcinoma and adenocarcinoma. This study seeks to find the disparity in the incidence, prevalence, aetiology, screening and presentation of cervical cancer between Africa and America.

Keywords: human papillomavirus, cancer, cervical, intraepithelial lesion

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Prevalence and incidence of cancer of the cervix

Global statistics on cancer shows that there were 570,000 fresh cases of cancer of the cervix with 311,000 mortalities in 2018. Of these new cases, 500,000 (88%) cases were from countries of low and middle income (CLMI) [1]. This ranks cancer of the cervix in terms of diagnosis (of cancer) as the fourth most frequently diagnosed. Globally among women, it is the fourth most frequent cause of death. However among CLMI cervical cancer ranks tops among causes of gynaecological malignancy and is regarded as second in the most implicated cause of malignancies among women trailing behind breast cancer.[1] Country to country, there exist differences in the occurrence and death rate of cancer of the cervix. Compared to women in developed countries, women in developing countries have a two to three times increase in incidence of cancer of the cervix and related deaths; hence accounting for over three quarter of the burden of this disease.[2–4]

Cancer of the cervix is the most common cancer occurrence in 28 countries and is the most frequent cancer-associated mortality in 42 countries among women, the bulk coming from sub-Saharan Africa.[1] Countries of low and middle income continues to experience an increase in incidence, prevalence, and mortality rates of cervical cancer while the rates are declining in developed countries.[1] Statistics from Kenya shows that among women aged 15–44 years cancer of the cervix is the most prevalent cancer, with an annual estimate of 4,802 women diagnosed and 2,451 mortality from the cancer. The high incidence and death rates can be ascribed to the lack of the human papilloma virus vaccine and the poor screening coverage. Furthermore, according to WHO, in 2030 there is expected to be an increase in cervical cancer mortality by 42% to 442,926 deaths. The highest increase will be in low and middle income countries where presently there is occurrence of 85% of incident cervical cancers and 87% of cervical cancer deaths.[5,6] However, given the gross under-reporting in many African countries, the true incidence of cervical cancer is unknown in Africa. Just few countries have functioning cancer registries and there is non-existent or minimal record-keeping. Some of the statistics stated in this literature are hospital-based, hence representing a small percentage of women who die from cancer of the cervix, as many women may not have access to hospital care and die at home.

In 2010, an estimate of 12,200 new cases of cervical cancer were diagnosed in the United States, leading to an incidence rate of 7.9/100,000 women.[7] There has been notable decline in the incidence of invasive cancer of the cervix over the last 35 years of cancer surveillance in the United States. However, this decline has not been similar for diverse racial groups and diverse histologic categories of cervical cancer. For cervical cancer screening recommendation, proper characterization of differences in decline by race and histological category is fundamental. However, there are detailed differential

decline done by previous studies based on histologic subtypes besides the adenosquamous subtype. 24 years has been the lengthiest duration for an analysis.[8,9]

Between 1973 and 2007, there were diagnosis of 37, 776 cases of invasive cervical cancer in the Surveillance, Epidemiology and End Results (SEER) Program registry dataset.[7] 45-49 year age group was the highest in the overall incidence of invasive cervical cancer. However, peak age group showed variation by histologic types. Squamous cell incidence peaked in the 45–49 year age group. 35-39 years were the peak ages for both adenocarcinoma and adenosquamous carcinoma.[10]

Factors responsible for the high incidence and prevalence of cervical cancer in Africa

Socio-economic factors

Worldwide, the chances of having cervical cancer are higher among women of low socio-economic status; hence why cancer of the cervix is often regarded as poverty disease and disease of poor women. Poor social states, high birth rate and poor hygienic conditions were the key co-factors for cervical cancer in a recent study in Mexico in which the populace was extensively infected by HPV.[11] Widespread conditions such as war, political chaos, internal conflicts and drought in Sub Sahara Africa fosters below standard living conditions. These factors often lead to displacement of people for certain period of time. Under such refugee-like state, vices such as rape, prostitution and recurrent marriages and cohabitation exist promoting the transmission of HPV. Sexual promiscuity is associated with war; this then contributes to the incidence of cervical cancer. A case–control study funded by Stanford University in 1996 recorded that the Vietnam War significantly contributed to the issue of cervical cancer in modern Vietnam, and that an all volunteer nonprofit organization called the Vietnam/American Cervical Cancer Prevention Project was created. Publication of data that links diseases to war was delayed for eight years. This was an effort to ease the process of resolution by offering what most would call a remedy in advance of what a few will perceive as being an accusation.[12] Most Sub Sahara African countries are situated within the Tropical Rain Forest with difficult topography; thus making access to screening, health education and treatment difficult.

Biological factors

Sub Saharan Africa is ravaged by poor nourishment and infections such as malaria, HIV and tuberculosis. This has lead to many being immuno-compromised. Some studies have showed the link between HIV and HPV. The prevalence of cervical intraepithelial neoplasia (CIN) has an estimate of as high as 20–40% in HIV-positive women.[13] HIV-positive women has the tendency to have continual HPV infections than those HIV-negative. HIV-positive women had a considerably higher prevalence of squamous intraepithelial lesion (SIL) in a study of 2,198 women who went to gynaecological clinics in Abidjan, Côte d'Ivoire.[14] A five-fold elevated risk of high-grade SIL among 513 women who were positive to HIV in a family planning clinic in Kenya was documented by Temmerman et al.[15] From the region, other reports illustrates that women with HIV have cancer of the cervix at earlier ages those HIV-negative.[16] In Kenya, Gichangi et al.[17] recorded that women under the age of 35 who had invasive cervical cancer had a 2.6 times chance to be HIV positive than controls of comparable ages (35% vs. 17%, OR 2.6, p=0.043). A published work from Tanzania showed that HIV-1 prevalence was higher amongst the cervical cancer patients (21.0%) than the controls (11.6%). HIV-1 was a potent risk factor for cervical cancer (OR=2.9, 95% CI=1.4–5.9).[18] 67% of the world population of humans living with HIV and AIDS are harbored in Sub-Saharan Africa.[19]

Lack of awareness and knowledge of cancer of the cervix in Africa

Cancer of the cervix is yet to be regarded as a serious public health problem in sub-Saharan Africa. In Sub Sahara Africa, importance is placed on infectious diseases such as malaria, diarrheal diseases, acute respiratory infections, tuberculosis, leprosy and HIV/AIDS each of which have strategies for prevention and to manage. Poor knowledge of cervical cancer in Africa has been shown by some studies, which cuts across a variety of literacy levels. In a maternal and child health clinic in Lagos-Nigeria which had 500 attendees, only 4.3% were aware of cervical cancer.[20] In 2004, still in Lagos-Nigeria, 81.7% of 139 patients with advanced cervical cancer had never heard of cervical cancer, and 20%, 30% and 10% respectively felt the symptoms they were experiencing where due to factors such as resumption of menses, irregular menses and lower genital infection. A good number of the women (98%) believed their advanced disease had cure, 12% thought it wasn't a serious disease and only 9% understood it was cancer; hence serious.[21] Similar studies in Tanzania and Kenya also documented very poor knowledge of the disease in patients.[17,22] Inadequate knowledge isn't restricted to patients only as health professionals who should be well informed don't have sound knowledge either of the disease. In Lagos Nigeria, an important factor why women present with late stage disease was found to be 'delay by primary health care workers in referral of cervical cancer cases'. An average of 9.35±12.9 months was taken for primary health care providers to make diagnosis and refer women with cervical cancer for management to a tertiary hospital.[20]

Improvement of knowledge and acceptance of preventive measures against cervical cancer is improved by education. A study in Northern Nigeria among 375 female university students based on 'awareness of cervical cancer and acceptance of HPV vaccine, 133 (35.5%) participants knew about HPV, cervical carcinoma had been heard by 202 (53.9%) and 277 (74.0%) were willing to receive HPV vaccination.[23] Apochie and colleagues[24] conducted a cross sectional survey in a university in Accra, Ghana among students 18 years of age and above. 157 students were selected as sample to study the beliefs and understanding about screening of cervical cancer. Generally, they appeared to have understanding about the benefits cervical cancer screening had. The believe that the test could locate changes in the cervix prior to them being cancerous was by Over 64% of respondents whereas, 78.5% felt such changes could be cured easily. Amongst the supposed screening barriers, the most common barrier was that diagnosis of cancer being the reason for cervical cancer screening was believed by just half of the respondents. The next most prevalent barrier (40.6%) was the belief that cervical cancer screening will not be permitted by their partner. There were other barriers such as: expense (23.2%), ignorance of where to go (24.3%), and thought of them being sexually active by people (24.6%). Positively, few believed the pap test would come with pain (9.4%). Whereas, over 68% perceived susceptibility of cervical cancer by young women possible, 52.5% believed they had the risk of cervical cancer themselves. 73% which constituted around 3/4 of respondents believed the cancer was so serious to the point of making a woman's life difficult and about 62% believed effective cures for cervical cancer existed of. Generally, a small percentage got from their social environment screening cues through screened peers or from the recommendation of healthcare workers. Of the fifteen respondents, only six who got a health care worker recommendation to get cervical screening, planned and got

one. The ones that reported receiving a recommendation but didn't go to be tested stated the following reasons: it was expensive; no knowledge of the location for screening; they felt embarrassed to be exposed to the screening and didn't have time to fix and get screening. 1/3 reported ever hearing a mass media talk on cervical cancer while a 1/5 have listened to at least a talk on cancer of the cervix at a church or other social congregation. About half stated the will to get the inexpensive option of cervical cancer screening (visual inspection and mild acetic acid), if a doctor recommended it. In general, awareness on issues linked to screening was good, though there existed particular gaps in knowledge about screening intervals and risk factors.

Etiology of cervical cancer

It has been established that an essential (though not adequate) cause of the development of cancer of the cervix is continual infection of the cervix with high-risk types of human papillomavirus (HPV).[25] According to evidence, cervical cancer development is preceded by HPV infection by several decades and that continual infection with HPV is a factor for the development and progress of pre-cancerous lesions of the cervix, to either higher grades of pre-cancerous disease or to invasive cancer. This process can take 10–30years.[26] After sexual activity commencement, a common sexually transmitted infection acquired is HPV. Within 1-2years, most HPV infections disappear on their own, although all persistent infections with high-risk types of HPV (especially HPV 16 and HPV 18) may advance to precursors of and eventually to invasive cervical cancer.[27] High-risk types of HPV are seen in nearly all cervical cancers, and cancer phenotype is importantly to retained by the HPV oncoproteins expression. The following twelve HPV types are classified by International Agency for Research on Cancer as carcinogenic to humans: 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, and 59. Worldwide, 70% of cancers of the cervix cases are accounted for by HPV16 and HPV18.[28]

Small geographical differences has been seen in the prevalence of the major HPV types related to cervical cancer, but the percentage of cancers in relation with types besides 16 and 18 is higher in high-risk locations.[28] A 38 countries study over a 60-year time frame which evaluated HPV infection in 10, 575 histologically verified cases of invasive cancer in Latin America and the Caribbean, Asia, Europe, Oceania, North America and Sub-Saharan Africa; using paraffin-embedded samples. The study showed 85% (n = 8977) positivity for HPV DNA.[29] The 8 most prevalent types of HPV found were 16, 18, 31, 33, 35, 45, 52, and 58; put together, they had a 91% contribution to the 8977 positive cases. The three most prevalent type of HPV were 16, 18, and 45 in each cervical cancer histological form (squamous cell, adenocarcinoma, and adenosquamous carcinoma), representing 61%, 10%, and 6%, respectively.

Unaided, HPV infection may not be enough for cervical cancer to develop; hence other factors may play a role in the development of this cancer.[30] High birthrate (over 6) is related to the risk of cervical malignancy amongst high risk HPV women. In Latin America, fertility has been proposed to have had an important role in decreasing the incidence of cervical carcinoma.[31] Similarly, a link between oral contraception and increased risk of cervical cancer has been established (RR, 1.9; 95% CI, 1.69–2.13). Dose–response analyses show that risk increases higher risks with longer period of usage [31]. Nonetheless, there is no relationship between the prevalence of contraceptive usage and incidence of cervical carcinoma in the available population based data.

Irrespective of the considerable increased risk of cervical carcinoma for current smokers (RR, 1.50; 95% CI, 1.35–1.66) and decline of risk after quitting smoking, the relationship between cervical malignancy and tobacco intake is confined to squamous cell carcinoma, and data on a dose–response remain debatable.[31] The relationship between HPV and other STI has been continually seen by confirmation from observational studies; especially Chlamydia trachomatis, herpes simplex virus type 2, and HIV. Additionally, Chlamydia trachomatis (OR 1.8) and herpes simplex virus type 2 (OR 2.2) have also been linked with an elevated risk of cervical carcinoma,[31] Regarding HIV, the existing information reports an apparent link of the co-infection and an elevated risk of cervical intra-epithelial neoplasia, whereas, there are reports of fewer consistent data towards invasive cervical cancer, partly because both diseases have high prevalence in high-risk countries for HIV.[32] Given their related dynamic of exposure and spread and their related social determinants, all of the above-mentioned infections are related.

Screening for cervical cancer

The development and testing of a variety of evidence based cervical cancer screening has been done, and are suitable for variety of contexts which include:

a) Cytologic screening via Papanicolaou (Pap) smear with follow-up colposcopy and biopsy to recognize early stage dysplasia and pre-cancers,

b) Clinician-sampled or self-sampling techniques testing of HPV

c) Visual inspection methods (using acetic acid and/or Lugol's solution), which are potent and cheaper method suitable for establishments with low-resource. Other screening methods can be complimented by visual inspection methods and their sensitivity and specificity have been shown to be enough in identifying later stage pre-cancer.

Cervical visual inspection with acetic acid (VIA) is the most commonly used screening approach implemented in settings resource-limited in CLMI.[33] To perform VIA, a vinegar solution is applied to the cervix then naked eye inspection is done to recognize precancerous lesions which are then treated via the loop electrosurgical excision procedure (LEEP) or freezing. The sensitivity of the VIA screening test is 82.4% (76.3% - 87.3%) and its specificity is 87.4% (77.1% - 93.4%).[34] This method is proven to be cost effective and harmless. Nevertheless, irrespective of the numerous screening modalities suitable for the context of low-resource, there is still insufficiency in global cervical cancer screening coverage.

Sub-Saharan Africa programs for cervical cancer screening have a poor coverage. A 57 countries study conducted in 2002 to access the extent of the programs of cervical cancer screening showed an effective coverage to be an average of 40%. Also, an average of 19% was seen when survey was done in 30 developing countries.[35] In the same vein, other researchers documented the cervical cancer screening coverage in sub-Saharan Africa as 2 to 20% for urban regions and 0.4 to 14% for the rural regions.[36] In sub Saharan Africa, women (60 to 80%) who develop cervical cancer stay in the rural areas where the chance of part taking in cervical cancer screening program doesn't exist.[37] Furthermore, women of high economic class have a better coverage of the screening. This still puts women in sub Saharan Africa among those with poor coverage because most are not of the high economic class. Similarly, a WHO publication from the work of Sankaranarayanan et al in 2001[33] pointed to the general lack of organized cervical carcinoma screening programs in sub-Saharan Africa. With all these, it is of little surprise why developing countries have 80% of death from cervical cancer [38]. On the flip side, reports

of numerous developed countries with proper cervical screening program having an increased percentage of adenocarcinoma of the cervix have been made.[39]

In incidence, mortality and screening of cervical cancer, key disparities persist. In the United States, incidence rate declines 1.9% per year and total cervical cancer mortality rate has being stable. By State, 5 states have a considerable incidence rate decrease; whereas other states had stability in incidence. The United States mortality rate and Incidence have stayed above the HP2020 targets, but are not far from them. A national survey data has shown that women that are updated with recent cervical cancer recommendation are upto 83% with a slight downward slope seen in the percentage of screened women within 2008-2010.[40] More improvement is needed toward the HP2020 objective for cervical cancer screening, particularly for women don't have access to health care due to absence of healthcare coverage or routine health care provider. According to the finding, in the past 5 years, an approximate of 1 in 10 women haven't been, this is inclusive of 1 in 4 women who didn't have health insurance and 1 in 4 who didn't have routine health care provider. Age, geography and race/ethnicity disparities exist in cervical cancer. While women of younger and older ages had comparable rates of no screening in the past 5 years, development or death from cervical cancer is uncommon in younger women in the USA.[41] The greater percentage of women aged >40 who are poorly screened is more worrying, they have the highest rates of incidence and death from cervical carcinoma. Death from cervical cancer are greater for black women; however, incidence rate are greater for Hispanic and black women when compared to white women.[42] As compared to other survey regions, the higher incidence and mortality rate and percentages of no screening in the past 5 years were documented in the south. The findings concerning geographic disparity supports other works with findings related to Appalachia, the lower Mississippi Valley, southeastern Atlantic states and along the United States–Mexico border.[43,44] Explanation may be afforded for some percentage screening disparities by financial and nonfinancial barriers. In the past 5years, from the approximately 8.2 million women who hadn't been screened, 69.9% were insured and had a routine health care provider, 9.6% had insurance but no regular health care provider, 9.8% had no insurance but had a routine health care provider, and 10.7% had neither. For over 20years, the National Breast and Cervical Cancer Early Detection Program (NBCCEDP) have been attending to these issues however its actions are still below expectations. About a third of women who were eligible for cervical cancer screening were reportedly not screened.[45] There is need to elucidate for health providers and for women the most potent method of screening due to the various age-dependent options for screening and changing technologies.

Presentation of cervical cancer

Irregular vaginal bleeding and discharge, presentation with pelvic pain and urinary or bowel symptoms by patients with advanced disease are the commonest symptoms of cervical cancer by patients [46]. The cancer locally spreads through the lymphatic system to the pelvic and para-aortic lymph nodes; although, it can metastasize to far-away organs—usually the lung, bone, liver and supraclavicular lymph nodes—through the hematogenous pathway. Intracranial metastatsis isn't unusual.[47,48]

Conclusion

There is a yawning gap in the incidence, prevalence, presentation and screening practices of cervical cancers between Africa and America for obvious reasons including a lack of purposeful surveillance programs in Africa, poor knowledge about the disease, poverty. African leaders must make deliberate efforts to fund screening programs aimed at identifying women at risk to receive intervention and preventing progression to cancer. This will help reduce the gap in the high rate of death from cervical cancers among our women relative to the Americans.

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Conflicts of interest

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