THE CHALLENGES OF HUMAN PAPILLOMAVIRUS AND CERVICAL CANCER THERAPY AND CONTROL IN NIGERIA: A REVIEW

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ABSTRACT
With the changing paradigm in disease trends, Nigeria may be faced with serious challenges in terms of healthcare and disease management. Cervical cancer, which is one of the cancers that is vaccine preventable, remain the most frequently reported and the leading cause of mortality from cancer in Nigeria. More than 36.59 million women are at risk and 26 die of the disease on daily basis. The country is currently ranked the worse place to be a woman with cancer in Africa, yet there is nothing to write home about in terms of preparedness. Every year huge amount of money is released but little or nothing gets done. There is urgent need for immediate action, especially with the advent of the three promising prophylactic vaccines, to be more pro-active, in controlling the menace of cervical cancer in the country. Cervical cancer should be given same priority as HIV/AIDs, Tuberculosis, Malaria and Childhood immunizations.
Key words: Cervical cancer, Challenges, Control, Human papillomavirus, Nigeria, Therapy.

INTRODUCTION
While viruses account for more than 20% of all cancers, human papillomavirus (HPV), the principal aetiologic agent of cervical cancer is responsible for about 5.2% of all infectious related cancers and almost all cases of cervical cancers(Munoz *et al.*, 2006). HPV infection is the most common sexually transmitted infection (Trottier and Franco, 2006; Dunne *et al.*, 2007; Gavillon *et al.*, 2010) affecting men and women (women much more at risk), even among those at lower risk of developing other sexually transmitted infections (Reed *et al.*, 1993; Zazove *et al.*, 1993; Baseman and Koutsky, 2005). More than 660 million people are infected with the virus globally (Brooks *et al.*, 2013) and Nigeria has a high incidence of sexually transmitted infections including human papillomavirus. Cervical cancer, the leading female cancer in Nigeria, arises when there is persistent infection with the high risk human papillomavirus, and this occurs in 5-10% of infected women (Bosch *et al.*, 2002).

Despite the fact that cervical cancer remained the only cancer that is vaccine preventable, it has reached a crisis level in Nigeria, claiming the lives of 9,659 womenout of 14,450 diagnosed annually (Mohammed *et al.*, 2008) and every 24 hours 26 women die of the disease(Olokor, 2014).Only 5% of women in Nigeria were screened for cervical dysplasia as compared to 40-50% in developed countries (Eke *et al.*, 2012). Services are only available in teaching hospitals and are not adequately utilized.

HPV infection and cervical cancer
Epidemiological and clinical studies have detected high risk human papillomavirus in practically 100% of cervical cancers (Bosch *et al.*, 2002). Equally, viral DNA was detected in the majority (70-90%) of cervical cancer precursor lesions (CIN-II and III) and in 20-50% of low grade lesions (CIN-I). In addition, even in uncertain lesions (ASC-US) the detection of HPV was close to 50% (Szostek *et al.*, 2008; Piras*et al.*, 2011). The fraction of cervical cancer attributable to HPV was very high (95-99%). These associations are among the highest ever identified in human cancerology, with a growing consensus existing in qualifying HPV as the necessary cause. Studies have demonstrated that persistent cervical infections with high risk HPVs precede the appearance of the precursor lesions and are required for the development, maintenance and progression of these lesions (Schiffman *et al.*, 1993; Bosch *et al.*, 1995).

Prevalence
Certain human papillomavirus types (especially 16 and 18) have been strongly associated with cervical cancer and its precursor lesions (Schiffman *et al.*, 1993; Bosch *et al.*, 1995).Nigeria has a population of 36.59 million women aged 15 years and above who are at risk of developing cervical cancer-the most frequent cancer among women aged 15-44 years (WHO/ICO, 2010) and the leading cause of cancer related deaths for women in developing countries, Nigeria inclusive (Faley, 2004; Agustin, 2007). However, there is no concrete data regarding the infection and onlya few studies were carried out in some smaller regions in the country.According to a study that was conducted in Ibadan South-Western Nigeria (Thomas *et al.*, 2004), among female population of Idikan community, a reported prevalence of 26.3% for the overall HPV infection was found, with about 75% of the infections coming from high risk types.

A similar study conducted in Okene, North-Central Nigeria reported a prevalence of 21.6%; and same high risk HPVs accounted for 77% of the infections (Pimentel *et al*., 2013). In addition, Auwal *et al*.(2013) recorded a prevalence of 76% for HPV types 16 and 18 among women in gynaecology clinics in Kano, North-Western Nigeria.

Burden

Nigeria and four other countries (India, China, Brazil and Bangladesh) have been identified as the most dangerous place to be a woman with cancer; making Nigeria to have the highest cancer death rate in Africa. Half of the women who die of cervical cancer live in these countries; which are responsible for 137,817 deaths compared to an estimated 274,883 from 529,409 new cases recorded in 50 countries (Ogundipe, 2013).

Every year the government releases huge amount of money for major awareness projects but little or nothing gets done. The Federal Government of Nigeria ironically, purchased screening equipment's worth $9 million, upgraded 20 active hospital-based cancer registries and trained medical personnel while NEMA acquired cobalt 4800 for the detection of high risk HPV types, yet the incidence of cervical cancer is on the high side (Ohai, 2012).

The primary screening tool for cervical cancer is cytology popularly known as Pap smear test which has been effective in reducing the incidence and mortality from the disease in many developed countries. It is cheap, easy to perform and has specificity as high as 99% (Faley *et al*, 1995). But this is difficult to achieve in our setting because of significant competing urgent health care needs; in particular the HIV epidemic and polio eradication issues and partly because of poor functioning health care delivery system.

To screen a woman for cervical dysplasia using the conventional Pap smear, a minimum of N700 is required in Aminu Kano Teaching Hospital in Northern Nigeria and up to N5000 in other centers in the country. Visual inspection of the cervix using acetic acid (VIA), another screening method cost atleast N1000 while cryotherapy including 1stdose of HPV vaccine cost up to N40000. A single dose of HPV vaccine is worth N20800 and a woman would need 3 doses over a period of 6 months. This is by far above the minimum wage of N18000 in the country. In a more complex situation a minimum of N500000 is required to manage a woman with cervical cancer, ranging from surgery, blood transfusion, radiotherapy, hospital admission, and other laboratory services excluding indirect expenses.

The polyvalent and bivalentHPV vaccines are major tools for primary prevention; the vaccines are attractive and cost effective, however, without International assistance it will become inaccessible to many Nigerians.

Recommendations

Screening and vaccination against HPV offers 100% prevention against cervical cancer. The World Health Organization position paper on HPV vaccination clearly outlines appropriate, cost effective strategies for using the vaccine in public sector program (WHO, 2009). The vaccines are expected to be cost effective way to reduce anogenital HPV infection, the incidence of cervical cancer and HPV-associated health care burden (Brooks*et al*., 2013). But the two vaccineseven if available offer protection against only 2 high risk HPV types (16 and 18) and some few low risk types which also causes papilloma (warts). In addition, the report of Clifford*et al*. (2005) and WHO (2005) suggest that HPV type 16 appear to play a smaller role in cervical cancer in Nigeria than in Europe.

There is urgent need for base-line community-based studies nationwide to determine the distribution pattern of prevalent HPV serotypes. Cervical cancer should be given same priority as HIV, TB, Malaria and childhood immunizations, while women should be encouraged to visit available facilities for early screening of pre-cancerous lesions and HPV testing/vaccination.

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