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A REVIEW ON ROLE OF HUMAN PAPILLOMA VIRUS IN CERVICAL CANCER AND ITS DIAGNOSIS

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Abstract— **During the 1990s, epidemiological studies supported by molecular technology, provided evidence on the causal role of some human papillomavirus (HPV) infections in the development of cervical cancer. Cervical cancer is an important public health problem among adult women. HPV testing was shown by several studies, In populations where cytology programmes are not efficient, HPV testing should now be considered as an alternative test for primary screening. Prevention of exposure to high risk HPV types by vaccination may prove to be the most efficient and logistically feasible preventive intervention for cervical cancer. Screening programmes are also more realistic and effective to target the screening on high-risk women once or twice in their lifetime using a highly sensitive test, with an emphasis on high coverage (>80%) of the targeted population. Lymph node status is the key to determining the prognosis and treatment of cervical cancer. However, it cannot be assessed clinically, and testing for nodal metastasis is controversial.**

Keywords: HPV, cervical cancer, cytology, VIA.

I. INTRODUCTION

Cervical cancer is an important public health problem for adult women in developing countries in South and Central America, sub-Saharan Africa, and south and south-east Asia, which is the most or second most common cancer among women (Prabhakar., 1992). The vast majority of cervical cancer are caused by infection with certain subtypes of human papilloma virus (HPV), a sexually transmitted virus, infects cells and may result in precancerous lesions and invasive cancer (zur Hausen.,1986).

Developing countries were accounted for 370 000 out of a total of 466 000 cases of cervical cancer that were estimated to occur in the world in the year 2000 Worldwide, cervical cancer claims the lives of 231 000 women annually, over 80% of whom live in developing countries(Franco.,1991).

A. Discovery and development

A major discovery in human cancer aetiology, that cervical cancer is a rare consequence of an infection by some mucosa tropic types of HPV. In public health terms, this finding is equally important as the discovery of the association between cigarette smoking and lung cancer, or chronic infections with hepatitis B virus (HBV) or hepatitis C virus and the risk of liver cancer (Prabhakar., 1992).In this HPV disease model, intense efforts are currently going into the development and testing of vaccines that may prevent the relevant HPV infections, and presumably, cervical cancer (Bosch.,1991).

The development of this technology to test for the presence of HPV DNA in cellular specimens in the early 1980s, the Evidence is also accumulating for HPV involvement in a considerable proportion of cancers of the vulva, vagina, anal canal, perianal skin, and penis (Bosch., 1991). The association of HPV with this cervical cancer has provided the background and the justification for improving screening programmes and for developing HPV vaccines (Thomas., 2001). The observations and Studies include prevalence surveys, natural history investigations, case–control studies and, more recently, a randomised intervention trial (Bosch., 1991).Natural history and follow up studies were clearly shown that HPV infection preceded the development of cervical cancer by several years and confirmed that sexual transmission is the predominant mode of HPV acquisition (Susser, 1973).

These studies satisfied, in biological terms, the long known clinical , epidemiological observations that cervical cancer displayed the profile of a sexually transmitted disease (STD) (Holowaty *et al.,* 1999).Case–control studies, case series, and prevalence surveys have unequivocally shown that HPV DNA can be detected in adequate specimens of cervical cancer in 90–100% of cases were compared with a prevalence of 5–20% in cervical specimens from women identified as suitable epidemiological controls (Susser., 1973). The aim of cervical cytology programmes is to detect precancerous lesions and treat them before they progress to invasive cancer (Susser., 1973). In contrast, the risks of disease and death from such lesions have remained largely uncontrolled in

high-risk developing countries, mostly because of the lack of screening programmes or else because of their ineffectiveness (Holowaty *et al.,* 1999). This paper reviews existing experiences, achievements, constraints, lessons and cervical cancer intervention programmes in developing countries. The sensitivity and specificity values that we will be reporting for various screening tests correspond to the detection of highgrade lesions (cervical intraepithelial neoplasia II and III) and invasive cancer (IARC., 1995).

B. Preventive interventions

Since the late 1980s, multiple studies have considered for HPV testing either as a triage test in cases of mild abnormalities or as a primary screening test.
(Campion., 1986). In brief, triage studies have shown that HPV testing is much more sensitive than repeated cytology in identifying underlying high grade lesions in women that reflect primary screening conditions (in the absence of fully randomised trials) have shown that the sensitivity of HPV tests is higher than standard cytology in detecting high grade lesions, whereas the specificity is age dependent (Cuzick., 1994).

C. Determinants of HPV infection

Epidemiological studies are investigating the risk factors for HPV infection clearly and consistently have shown that the key determinants among women are the number of sexual partners, the age at which sexual intercourse was initiated, and the likelihood that each of her sexual partners was an HPV carrier. These are lifelong behavioural traits, thus clearly preceding the development of cervical cancer (Barrasso., 1987).

The role of men as possible vectors of HPV was measured in the early epidemiological studies that asked about the sexual behaviour of the husbands or sexual partners of patients with cervical cancer and controls (Fahey *et al.,* 1995). In addition, many recent studies had the ability to measure HPV DNA in exfoliated cells from the penile shaft, the coronal sulcus, and the distal urethra (Barrasso., 1987). In populations where female monogamy is dominant, the population of female sex workers plays an important role in the maintenance and transmission of HPV infections (Beral., 1974).

D. Cervical cytology screening programmes worldwide

To date, cervical cancer prevention efforts worldwide have focused on screening sexually active women using cytology smears and treating precancerous lesions (Beral., 1974). It has been widely believed that invasive cervical cancer develops from dysplastic precursor lesions, progressing steadily from mild to moderate to severe dysplasia, then to carcinoma in situ, and finally leads to cancer (Nasiell *et al.,* 1986).

Even though the impact of cytology screening has never been proved through any randomized trials, it has been shown to be effective in reducing the incidence and mortality from cervical cancer in developed countries (Biermal., 1998). Many national guidelines are currently moving towards less frequent smear tests (once every 3–5 years) because it is recognized that this cervical lesions develop slowly over several years (Nasiell *et al.,* 1986). Women with low-grade lesions were generally advised to return for routine follow-up smears. Women with high-grade precursor lesions were further evaluated via colposcopy, biopsy, and subsequent treatment of confirmed lesions (Holowaty *et al.,* 1999).

Organized programmes with systematic call, recall, follow-up and surveillance systems that are shown the greatest effect (e.g. in Finland and Iceland), even though they use fewer resources than unorganized programmes (e.g. in the USA)(Holowaty *et al.,* 1999). Cervical cytology is considered to be a very specific test for high-grade precancerous lesions but, even if the quality of collection and spreading of cells, fixation, and staining of smears, and reporting by well-trained technicians and cytopathologists are good, its sensitivity is moderate (Hakama *et al.,*1985).
The results of meta-analyses suggest that cytological screening has a very wide range of sensitivity for detecting lesions; assuming that cytology is only moderately sensitive, it seems likely that the observed decline in the risk of cervical cancer in developed countries may have arisen from the high screening frequency (Nanda *et al.,* 2000).

E. Cervical cancer screening programmes in developing countries

Cytology-based screening programmes for cervical cancer have been introduced in some developing countries, particularly in the region of South and Central America, over the last 30 years, but generally have achieved very limited success. In contrast, a comparison of the performance of conventional cytology and its potential alternatives in detecting cervical cancer and its precursors is on-going in Asia, Africa, and Latin America (Nanda *et al.,* 2000).Both these approaches are briefly reviewed below since they provide potentially useful information for directing public health policy on introducing new, effective programmes in low-resource settings and for reorganizing existing programmes (Irwin *et al.,* 1991).

F. Effective screening programmes in developing countries

Considerable discussion is focused on which screening test to use — cytology or alternatives to cytology, such as VIA or HPV testing, which combinations sequence of screening tests should be used for screening in developing countries (Nanda *et al.,* 2000). Choosing a suitable screening test is only one aspect of a screening programme. A more fundamental and challenging issue is the organization of the programme in its totality (Irwin *et al.,* 1991). Whichever screening test is to be used, the challenges in organizing a screening programme are more or less the same (Cuzick., 1992). However, screening tests (e.g. cytology, HPV testing) require additional recalls and revisits for diagnostic evaluation and treatment may pose added logistic difficulties and these may emerge as another barrier for participation in low-resource settings (Hakama *et al.,* 1986).

The choice of screening test in countries/ regions that plan to initiate new programmes should be based on the comparative performance characteristicsof cytology and its potential alternatives such as VIA, their relative costs, technical requirements, the level of development of laboratory infrastructure,feasibility in a given country/region (Hakama *et al.,* 1986).

If a potential alternative to cytology, such as VIA, is chosen for screening, considerable attention will be given to the proper monitoring and evaluation of the programme inputs and outcomes before further expansion (Cuzick., 1992). since VIA is still an experimental option for cervical cancer screening and it remains to be demonstrated whether VIA-based screening programmes are associated with a reduction in cervical cancer incidence and mortality, (Irwin IR et al.,1991). In developing countries, existing ineffective cytology based programmes will be urgently reorganized and monitored (Prabhakar., 1992).

In recent years, the use of magnetic resonance imaging and computed tomography to determine lymph node status has increased (Prabhakar., 1992).The accuracy of magnetic resonance imaging, computed tomography , positron emission tomography has been assessed previously in reviews, but updates are required because recent studies have reported on their diagnostic accuracy and on quality assessment in diagnostic reviews (Murthy *et al.,* 1993).

II. DISCUSSION

At the current level of knowledge, the causal role of HPV and its infections in the development of cervical cancer and its precursors has been proved. A large number of human studies were conducted and the evidence available at this time. Programmes for organized screening of cervical cancer are spontaneous screening involve substantial costs to provide for the associated infrastructure, manpower, consumables, follow-up, and also surveillance. Many low-income developing countries, particularly most of those in sub-Saharan Africa, currently having financial and manpower resources. Low income developing countries should consider planned investments in order to improve the capacity of their health services to diagnose and treat cervical cancer precursors and early invasive cancers, before considering even limited screening programmes. VIA may be considered as a suitable early detection test in the context of early clinical diagnosis in low income countries, particularly in those regions without extensive cytology laboratory facilities. Middle-income countries without any programmes for cervical cancer screening, but planning to implement such a programme, should consider organizing and sustaining it in a limited geographical region before expanding to cover a wider area. Managerial guidelines are now available to help in planning and implementing appropriate programmes in low-resource settings.

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References

[1] Prabhakar AK. Cervical cancer in India strategy for control. Indian Journal of Cancer, 1992, 104: 29–32.
[2] Murthy NS et al. Estimation of reduction in life-time risk of cervical cancer through one life-time screening.Neoplasma, 1993, 40: 255–258.
[3] Miller AB. Cervical cancer screening programmes—Managerial guidelines. Geneva, World Health Organization, 1992.
[4] Holowaty P et al. Natural history of dysplasia of the uterine cervix. Journal of the National Cancer Institute, 1999, 91: 252–268.
[5] Fahey MT et al. Meta-analysis of Pap test accuracy. American Journal of Epidemiology, 1995, 141: 680–689.
[6] Nanda K et al. Accuracy of the Papanicolaou test in screening for and follow-up of cervical cytologic abnormalities: a systematic review. Annals of Internal Medicine, 2000, 132: 810–819.
[7] Hakama M et al. Evaluation of screening programmes for gynaecological cancer. British Journal of Cancer, 1985, 52: 669–673.
[8] National Cancer Institute. Cervical cancer. Bethesda (MD): The Institute. Available: www.cancer.gov/cancertopics/types/cervical (accessed 2008 Feb 21).
[9] Nasiell K et al. Behaviour of mild dysplasia during long-term follow-up. Obstetrics and Gynaecology, 1986, 67: 665–669.
[10] Arbyn M, Raifu AO, Ferlay J. Burden of cervical cancer in Europe. Ann Oncol 2007;18:1708-15.
[11] Hatch K. Cervical cancer. In: Berek JS, Hacker NF, editors. Practical gynecologic oncology. 2nd ed. Baltimore: Williams & Wilkins; 1994. p. 243-85.
[12] Ho GYF, Biermal R, Beardsley L, et al. Natural history of cervicovaginal papillomavirus infection in young women. N Engl J Med 1998;338:423–28.
[13] Koutsky LA, Holmes KK, Critchlow CW, et al. A cohort study of the risk of cervical intraepithelial neoplasia grade 2 or 3 in relation to papillomavirus infection. N Engl J Med 1992;327:1272–8.
[14] Ho GYF, Burk RD, Klein S, et al. Persistent genital human papillomavirus infection as a risk factor for persistent cervical dysplasia. J Natl Cancer Inst 1995;87:1365–71.
[15] Remmink AJ, Walboomers JM, Helmerhorst TJ, et al. The presence of persistent high-risk HPV genotypes in dysplastic cervical lesions is associated with progressive disease: natural history up to 36 months. Int J Cancer 1995;61:306–11.
[16] Nobbenhuis MAE, Walboomers JMM, Helmerhorst TJM, et al. Relation of human papillomavirus status to cervical lesions and consequences for cervical-cancer screening: a prospective study. Lancet 1999;354:20–5.
[17] Rozendaal L, Walboomers JM, van der Linden JC, et al. PCR-based high-risk HPV test in cervical cancer screening gives objective risk assessment of women with cytomorphologically normal cervical smears. Int J Cancer 1996;68:766–9.
[18] Schlecht NF, Kulaga S, Robitaille J, et al. Persistent human papillomavirus infection as a predictor of cervical intraepithelial neoplasia. JAMA 2001;286:3106–14.
[19] Zielinski GD, Snijders PJF, Rozendaal L, et al. High-risk HPV testing in women with borderline and mild dyskaryosis: long-term follow-up data and clinical relevance. J Clin Pathol 2001;193:1–8.
[20] Campion MJ, McCance DJ, Cuzick J, et al. Progressive potential of mild cervical atypia; prospective cytological, colposcopic, and virological study. Lancet 1986;2:237–40.
[21] Cuzick J, Terry G, Ho L, et al. Human papillomavirus type 16 DNA in cervical smears as predictor of high-grade cervical cancer. Lancet 1992;339:959–60.
[22] Cuzick J, Terry G, Ho L, et al. Type-specific human papillomavirus DNA in abnormal smears as a predictor of high-grade cervical intraepithelial neoplasia. Br J Cancer 1994;69:167–71
[23] Rousseau MC, Franco EL, Villa LL, et al. A cumulative case-control study of risk factor profiles for oncogenic and non-oncogenic cervical human papillomavirus infections. Cancer Epidemiol Biomarkers Prev 2000;9:469–76.
[24] Kjaer SK, Chackerian B, Van den Brule AJC, et al. High-risk human papillomavirus is sexually transmitted: evidence from a follow-up study of virgins starting sexual activity (intercourse). Cancer Epidemiol Biomarkers Prev 2001;10:101–6.
[25] Barrasso R, de Brux J, Croissant O, et al. High prevalence of papillomavirus-associated penile intraepithelial neoplasia in sexual partners of women with cervical intraepithelial neoplasia. N Engl J Med 1987;317:916–23.
[26] Castellsagué X, Bosch FX, Muñoz N, et al. Male circumcision, penile human papillomavirus (HPV) infection and cervical cancer. N Engl J Med Rigoni-Stern. Fatti statistici relativi alle malattie cancerose. Giorn Prog Patol Terap 1842;2:507–17.
[27] Beral V. Cancer of the cervix: a sexually transmitted infection? Lancet 1974;i:1037–40.
[28] Skegg DC, Corwin PA, Paul C, et al. Importance of the male factor in cancer of the cervix. Lancet 1982;2:581–3.
[29] Schiffman MH. New epidemiology of human papillomavirus infection and cervical neoplasia. J Natl Cancer Inst 1995;87:20.
[30] Walboomers JMM et al. Human papillomavirus is a necessary cause of invasive cervical cancer worldwide. Journal of Pathology,1999, 51: 268–275.
[31] Ferlay J et al. Globocan 2000. Cancer incidence, mortality and prevalence worldwide, version 1.0. Lyon, International Agency for Research on Cancer, 2001 (IARC Cancer Base No. 5).
[32] ColemanMet al. Time trends in cancer incidence and mortality. Lyon, International Agency for Research on Cancer, 1995 (IARC Scientific Publications No. 121).
[33] Wabinga H et al. Trends in cancer incidence in Kyadondo County, Uganda, 1960–1997. British Journal of Cancer, 2000,82: 585–1592.