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Double jeopardy: HIV and cervical cancer in Indian women

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The ever-increasing number of women getting infected and dying from the human immunodeficiency virus (HIV) is a poignant feature of the worldwide expanding AIDS epidemic. The country widely projected to be the hardest hit in the next wave of the AIDS epidemic is India, where over 40% of the 5 million people living with HIV/AIDS in 2003 were women(1). The Indian HIV epidemic has grown from a concentrated epidemic among high-risk population subgroups like female commercial sex workers and injection drug users (prevalence in whom has consistently remained between 20 and 60%) to an almost generalized epidemic with many states approaching the general population prevalence of greater than 1% (2). India accounts for 10% of global HIV burden and 65% of that in South and Southeast Asia. Nearly 85% of transmission of HIV in India is heterosexual, and millions of married monogamous women now stand at enormous risk for acquisition of HIV through their spouses. In addition to lacking access to adequate primary health care, millions of such women in India are also vulnerable to multiple reproductive health problems including unplanned pregnancies and immediate and delayed complications of sexually transmitted infections. Given India's gigantic population of over 1 billion, even a 1% point increase in the HIV prevalence rate in the general population can translate to greater than 10 million new infections in absolute numbers, a scenario that can spell a national and an international catastrophe.

The soaring rates of HIV in India and lack of access to life-prolonging highly active antiretroviral therapy (HAART) have drawn worldwide attention from the government, bilateral and multilateral aid agencies, and the philanthropic community(3). Due to multiple global initiatives, the cost of HAART has fallen dramatically in the last 5 years. In collaboration with the UN-sponsored Global Fund, the Indian government has also announced plans for making HAART widely available and accessible to those most at need for the drugs(4). Access to treatment for opportunistic infections like tuberculosis is also expected to increase as a result of continuing funding mobilizations. As a result, an ever-increasing number of persons living with HIV/AIDS in India are poised to access affordable medications which may prolong their lives and prevent an immediate "death sentence."

While the AIDS epidemic soars in the country, more than 70,000 Indian women annually succumb to human papillomavirus (HPV)-induced cervical neoplasia, which is the commonest cause of cancer-related mortality in Indian women(5). This number is more than three times the combined number of cervical cancer deaths in all western countries and is equal to the combined number of such deaths estimated in China plus all of Sub-Saharan Africa(5). Additionally, more than 125,000 of the 470,000 incident cases of cervical cancer worldwide occur in India alone. Clearly, the country faces one of the greatest burdens due to cervical

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cancer than any other nation. Cervical cancer is entirely preventable through early detection, screening, and treatment. Yet, cervical cancer prevention and treatment services are woefully inadequate in the country and often compete with other public health priorities for funding and implementation. In addition to widespread ignorance and lack of awareness about the disease risk and prevention, programmatic factors which contribute to the high incidence and mortality due to cervical cancer include lack of well-equipped laboratories and trained technical personnel, inefficient referral systems, loss to follow-up due to low patient return rates, and limited tertiary and palliative care facilities(6).

The burgeoning AIDS epidemic is now superimposing on the high rates of cervical cancer incidence and mortality in India. HIV-infected women represent one of the highest risk groups for the development, progression, and recurrence of HPV-induced cervical precursor lesions and cervical cancer(7–9). Multiple studies(10–12) from across the globe as well as from India (13) have clearly demonstrated that HIV-infected women are two to five times as likely as HIV-uninfected women to manifest with cervical intraepithelial neoplasia and cervical cancer. There is limited, yet mixed, evidence(14–20) from global literature about the impact of HAART on evolution of cervical lesions in HIV-infected women, with many studies suggesting that HAART may not have a beneficial impact on regression of cervical preneoplastic and neoplastic lesions(18–20). In fact, it has been suggested that HIV-infected women who live longer as a result of HAART therapy might be at increased risk for prolonged exposure to HPV oncoproteins and thus be at increased risk for the acquisition of the molecular changes characteristic of carcinoma *in situ* that are necessary for progression to invasive cervical cancer (21). Irrespective of the impact of HAART on prognosis of cervical lesions, HIV-infected women need screening at frequent intervals and greater follow-up for the prevention of cervical preneoplastic lesions than HIV-uninfected women(22,23). HIV-infected women in India, who in the near future may get access to HAART and live longer than ever before, may therefore need a “continuum of care” and frequent reevaluations that could impose an additional economic burden on families and the health care system. The expanding HIV/AIDS epidemic thus represents a double-jeopardy situation for Indian women already at higher risk for developing cervical cancer in their lifetime than women in other parts of the world.

Unfortunately, resource-limited settings such as India and other developing countries present unique challenges for the planning and implementation of organized screening programs that are dependent on skilled manpower and sustained resources(22). Prevention of cervical cancer should therefore include consideration of alternative screening modalities including low-cost techniques like the “visual inspection with acetic acid” test (which can be taught to nurse midwives, provides on-the-spot results and can link diagnosis to treatment in the same clinical visit)(24); as well as modern technological advances like the liquid-based cytology (to improvise on the detection rates of conventional cytology)(25,26), automated cytology (to prevent procedural and reading errors in conventional cytology, and to overcome the lack of trained cytotechnologists)(27), and HPV testing (for triage of women with abnormal Pap smears)(28) using self-administered swabs (for ensuring privacy and thereby improving uptake of screening)(29). A potential HPV vaccine that might protect from “high-risk” HPV subtypes could be the ultimate prevention tool and may be on the horizon in the years to come. Evaluating the performance and cost-effectiveness of these adjunct or alternative prevention strategies in HIV-infected women in clinical and field settings should thus be priorities for scientists and policymakers(30,31). Invasive cervical cancer is an AIDS-defining condition, and because many women in developing countries present only in the late stages of the disease in absence of organized screening programs, it is often the very first sign of AIDS in these women. Thus, there exists a potential role of offering HIV testing for selected high-risk groups of women presenting with cervical neoplastic conditions, although this approach has yet to be validated rigorously in other resource-limited settings with similar general population prevalence of HIV

(32). However, with increasing population HIV prevalence in settings like India, this approach merits investigation.

The integration of cervical cancer prevention in the clinical management of HIV-infected women in India and other developing countries is thus a compelling priority. Strengthening cancer screening, treatment, and care services needs to be prioritized through increased funding, mobilization, and public awareness. Alleviating the impact of the double jeopardy of HIV and cervical cancer will require a reevaluation of current strategies, developing guidelines for improving preventive clinical care, and refocusing of efforts to combat both diseases affecting millions of women in India.

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