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Short Report

Optimizing cervical cancer care in resource-constrained developing countries by tailoring community prevention and clinical management protocol

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ABSTRACT

Cervical cancer is the commonest malignancy among women in resource-poor low- and middle-income countries (LMICs). Western models of health-care organization and delivery may not be suitable for these settings. Research in health services needs to be undertaken before Western oncological prevention and management protocols can be adopted from the innovative affluent countries. It is possible to tailor cervical cancer prevention and management protocols and to avoid inappropriate technology on the basis of a literature review of demographic and clinical profiles in LMICs.

Introduction

Cervical cancer is one of the commonest malignancies and causes of cancer death in less-developed regions of the world, with age-standardized incidence and mortality rates of 17.7 and 9.7 respectively. Every year, more than 80% of new cases and consequent deaths occur in the developing regions of the world. With 134,420 new cervical cancer cases and 72,825 deaths reported by GLOBOCON 2008, India accounts for more than a quarter of the global burden of cervical cancer [1]. A wide variation in incidence rates and differential clinical profiles of cervical cancer between nations and geographical regions suggests a role for environmental factors in etiology, pathogenesis and progression. Human papillomavirus (HPV), poor genital hygiene, patterns of sexual behavior, cultural factors, socio-economic factors (education and income), smoking, and a diet deficient in vitamin A are some of the causal associations and etiological risk factors of cervical cancer. Lower socio-economic status (SES) may be associated with lack of awareness of genital hygiene, indulgence in high-risk sexual activities and subsequent acquisition of sexually transmitted HPV infection, and development of pre-neoplastic changes (dysplasia and cervical intraepithelial neoplasia grades I through III) with gradual progress to invasive cervical cancers (coherence of association) [2]. HPV has occupied a central position in the etio-pathogenesis of cervical cancer since high-risk HPV DNA is consistently identified in formalin-fixed paraffin-embedded tissue specimens, small pre-neoplastic lesions, and also in cervical scrapes (temporal association and specificity of association, consistency of association) [3]. Disruption of the E2 gene of the host caused by integration of HPV DNA in the genome of infected subjects leads to the production of E6 and E7. Accumulation of multiple mutations and cervical cancer are the sequential outcomes of interference of E6 and E7 onco-proteins with the tumor suppressor function of p53 and pRB (biological plausibility) [4]. The germ theory of disease (Koch's postulate) insists that the cause must be both necessary and sufficient for the occurrence of the disease before it can be qualify as the cause of that disease. However, the association between HPV and cervical cancer fails to satisfy the criterion of a one-to-one causal relationship of Koch's postulate, as HPV is a necessary but not a sufficient cause of cervical cancer. Although HPV falls short by the criterion of a direct causal association with cervical cancer, it completely fulfills additional criteria for judging causality, i.e., temporal association, strength of association (higher relative risk of cervical cancer in HPV-infected individuals), specificity of association (further strengthened by the discovery of HPV DNA in malignant neoplasms elsewhere in body), consistency of association, biological plausibility, and coherence of association, thereby firmly establishing HPV as the major contributing factor in the pathogenesis of cervical cancer [2].

Like any other chronic ailment, cervical cancer is also associated with many other risk factors and cofactors. These factors may act additively or synergistically with HPV in cervical carcinogenesis

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(multifactorial association). Other risk factors and cofactors per se may not be carcinogenic in the absence of HPV, and HPV alone may not be a sufficient etiological factor in transforming normal cervical mucosa cells into atypical, dysplastic, pre-neoplastic and invasive cervical cancer cells. Critical biochemical events of the interaction between HPV and other risk factors and cofactors at the cellular level have yet to be elucidated. Emphasis on SES improvement could be a major path-changer in epidemiology, public health and clinical management of cervical cancer, as SES has a bearing on many of the risk factors and cofactors of the disease. Epidemiological studies have demonstrated that cervical cancer incidence and mortality reduce with the advancement of SES, i.e., affluent nations have a lower incidence and mortality as a function of SES [2]. Almost all of the hungry people and one third of 870 million people living below the poverty line live in developing regions of the world, and India may account for >80% and >25% of the global cervical cancer burden (incidence and mortality, respectively) [5]. Incidence and mortality rates have an inverse relationship with socio-economic status even within the confines of territorial boundaries. Incidence, mortality from cervical cancer, and utilization of the Papanicolaou (Pap) smear for early detection of cervical cancer differ across social groups even in developed nations. For example, American black and Hispanic women have a higher risk of developing cervical cancer and are more likely to die of the disease compared to Caucasian (white) women. American women of lower SES are also at risk of missing annual cervical cancer screening cytological examination and consequent early detection of their genital cancers [6,7]. It is very clear from the preceding discussion that SES determines the utilization of preventive oncological services, incidence, pattern, and survival of cervical cancer in economically advanced countries. Lack of adequate health infrastructure, low priority for research, poor documentation, absence of a population-based cancer registry, improper implementation of programs for collection of cancer data and statistics, corruption, social and civil disturbances in low- and middle-income countries, sole focus on treatment of cancer patients with very little emphasis on prevention and early detection, concentration of cancer care resources in metros and city complexes, all contribute to the socio-economic difficulties of people and compromise the optimum management of cervical cancer in economically emerging nations. Unlike the West, developing countries have made very little progress in designing and conducting research enquiring into various issues encountered by cancer patients in accessing anticancer, supportive, palliative and rehabilitation services. The huge burden of disease, the low budgetary allocation for health care, the consumption of a significant amount of resources in managing communicable diseases, mounting social issues of gender violence, crime, corruption, an increasing population, and poverty are responsible for the constantly shifting focus of media, policy-makers and legislators [8–11]. A multitude of social issues are responsible for lack of attention, easy distractibility, disorganization, procrastination and forgetfulness on the part of public health decision-makers. As a consequence, the growing problem of cancer and its prevention and control has not come under the scrutiny of media, policy-makers and legislators in developing countries. Overloading of an already constrained health-care system is the outcome of inequitable distribution of health resources, and many cancer patients die in the community because of poor access to cancer treatment facilities and the unaffordability of expensive anticancer therapy for a large majority of the poor masses [12]. Western models of organization of health-care systems and sophisticated prevention and management protocols of affluent nations have further worsened the scenario. Research and evaluation of prevailing health services in the current socio-economic climate has always been overlooked or, at the most, taken a back seat. Health-system organization, laboratory investigation work-up, therapy schema, follow-up protocols, treatment techniques, cancer management devices and equipment of socio-economically advanced countries have been adopted without extensive subjection of cancer health services to independent and combined pre-adoption or post-adoption evaluation for relevance, adequacy, accessibility, acceptability, effectiveness, efficiency and impact [11].

Socio-economically backward regions of the world have >80% of Earth's population, and this may correspond to 72.80% of the global cases of cancer in these less developed regions [5]. Low- and middle-income countries (LMICs) are also battling population expansion, very low budgetary allocation for health, communicable diseases, insanitation, poverty, corruption, unmet reproductive maternal and child health needs, and lack of universal primary prevention and health-care coverage. Most of the deaths in developing countries are due to infectious diseases, and malnutrition can be prevented by a dedicated and realistic national program. Nevertheless, infectious diseases, malnutrition and maternal and child health continue to claim their toll in spite of the existence of a national health program from as early as 1960s. Under-developed, ill-prepared health-care infrastructure is far from satisfactory to battle even the commonly prevalent and prioritized public health issues [11]. The proportion of chronic illness and death is much higher in higher-income countries than in LMICs. Cancer, globally, kills more people each year than acquired immunodeficiency syndrome (AIDS), malaria and tuberculosis combined. Nevertheless, cancer has hardly found a place in the World Health Organization's list of top ten causes of death, despite the colossal burden of cancer in these economically constrained nations [13]. Another disturbing fact is that the LMICs have to battle 80% of the global cancer burden with just 5% of the total cancer finances [14]. The US spent 17.8% of its GDP of approximately 15.68 trillion USD in the year 2011 for the health care of its people, in sharp contrast to 4.1% of 1.842 trillion USD in the year 2012 [15]. Considering the population of the US to be roughly around one third of that of India, the US spends around 140 times more per capita on health care of Americans compared to that of India. Low health-care spending of LMICs is the consequence of interplay between a number of social/economic/cultural/geopolitical factors, and nothing explains this phenomenon better than the following. Continuously expanding populations, huge dependence on life-subsistence, lower productive traditional occupations, insufficient numbers of technical and higher educational centers to reap the benefit of economic transition and globalization, unemployment, underemployment, a dearth of capital goods such as factories, equipment, machinery and public utilities, ill-equipped and poorly productive labor forces, inability to generate domestic capital or to save substantial amounts of domestic output, and corruption in the form of capital flight to tax havens in economically more advanced countries – all these factors have critically shrunk the financial base of the less developed countries, thereby severely impairing expenditure on public health care [8]. People in immediate need of life-saving medical treatment have to resort to out-of-pocket spending for treatment of their illness. People selling their assets or borrowing money from money-lenders at very high interest rates to pay for treatment of their medical conditions are well documented in India. India also has one of the highest out-of-pocket spending on health in the world, and nearly 5% of the Indian population (39 million people) are pushed into poverty each year by out-of-pocket health-care expenditure. Over the prevailing background socio-economic disadvantages, the health-care system in India is responsible for mounting woes on already distressed families, further disempowering people and trapping future generations into a vicious cycle of poverty because of their health conditions [12,16,17].

It is also very sad that most of the medical journals, irrespective of impact factor, publish articles demonstrating the superiority