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Cervical cancer outbreak in India – A review

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Abstract

Cervical cancer remains a significant public health issue in India, where it is one of the leading causes of cancer-related deaths among women. Cervical cancer, unlike an infectious disease, does not spread from person to person but is primarily caused by persistent infection with high-risk types of the human papillomavirus (HPV). It is estimated that about 1 in 53 Indian women will develop cervical cancer in their lifetime, compared to 1 in 100 women in more developed regions. vaccination coverage in India remains low due to various factors, including awareness, accessibility, and cultural beliefs. The challenges in combating cervical cancer in India include low awareness about the disease, limited access to healthcare facilities, socio-economic barriers, and stigma associated with gynecological issues. Increasing awareness about HPV vaccination, improving access to screening, and addressing cultural and socio-economic barriers are essential steps to reducing the burden of cervical cancer in India.

Key words : Cervical cancer, Human papillomavirus (HPV), Carcinoma, adenocarcinoma.

Cervical cancer :

It is the second most frequent cancer after breast cancer affecting women aged 15-44 years, globally. The vast majority of cases (99%) are linked with a sexually transmitted viral infection caused by human papillomavirus (HPV). Cervical cancer is a developed country's disease, largely preventable and treatable if detected early through regular screening. The success of any screening program depends on high coverage and equally important is the effectiveness of safe and affordable treatment for those who are tested positive. Preventative cancer through screening and vaccination could reduce 80% of cervical cancer morbidity and mortality worldwide. Enable timely health-seeking behavior equipping girls with relevant education, appropriate knowledge, and ensuring

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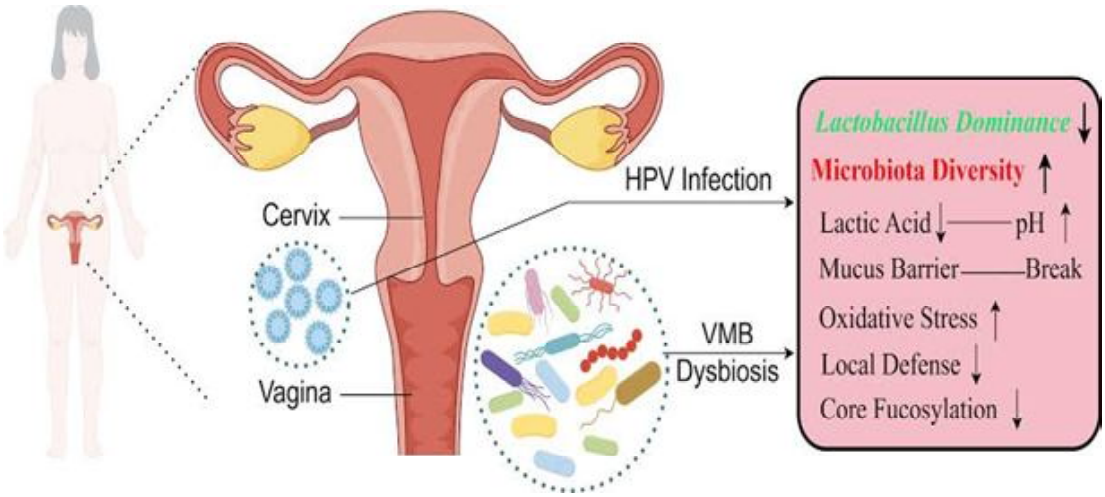
access to health care. The vast majority of full-blown cases more likely could be averted if prevention, early diagnosis, and timely intervention be in action. HPV vaccines are safe and highly effective against the virus strains that cause about 70% of cervical cancers. The primary aim of these vaccines is to provide protection and infection throughout life. As of today, only cervical cancer vaccination has been included in the National Immunization schedule as adopted by a few states in India. To put India on an informed path of preventing cervical cancer and other HPV-related cancers through vaccination screening, and preventing other HPV-related diseases like HPV types that cause: Anogenital, papillomavirus, Humanaccination, Cervical. There are two main types of cervical cancer namely squamous cell carcinoma and adeno-carcinoma.

Epidemiology of cervical cancer in India :

Cervical cancer is on the declining trend in India because it's vast increasing in population and it continues to be a major health problems to the women's in India. Cancer of the cervix has been the most important cancer among women in the past two decades. The recent NCRP data show that between 2009 and 2011 Aizawl district in the north eastern part of India had the highest levels of cervical cancer at an age-adjusted rate of 24. The annual percentage decrease ranged from a minimum of 1.3% in Bhopal to 3.5% in Chennai in the years from 1982 to 2010 [14]. Causes of cervical cancer include HPV infection, use of oral contraceptives, age of marriage, parity and exposure to cigarette smoke[11]. Several factors including sexually transmitted infections, reproductive factors, hormonal influences, genetic and host factors are responsible for the incidence of cervical cancer[50]. It is a significant public health burden in most developing countries, where it is a major cause of mortality and morbidity among women[15]. Majority of the participants 185 (71.4%) were aware that cervical cancer is one of the most wide-spread gynecological cancers in Asia. The awareness of causative agents of cervical cancer was known to 53.9% of the undergraduates and 50% of the faculty members. 73% of the total study groups have heard of HPV and around 68% agreed that it was detectable. 71% of the study sample had heard about the Pap smear test and 42% have undergone the test. The questions pertaining to the preventive measures of cervical cancer had good faculty preponderance with 91.8% giving a positive response. 84.1% of the students and 79.5% of the faculty members knew that abnormal vaginal bleeding was a symptom[1]. The Malwa region, commonly known as the cotton belt of Punjab comprising Bathinda, Mansa, Muktsar, Patiala, Sangrur among other districts is witnessing the steep rates in cancer cases. It has the highest average of 136 cancer patients per 1 lakh people which is exceeding the national average of 80 per lakh[44]. Despite being a preventable cancer burden, cervix cancer remains an important public health problem in India. Major reasons behind this are lack of awareness both in the health care providers and community as well as availability of the resources at all the levels of the existing health care system[29]. Of the 230 cervical patients included, 70% were from rural areas and the majority presented at Stage III and IV. Additionally, 173 out of 230 patients previously had gynaecological problems, of which more than 50% did not initially seek any



treatment. The common reasons for not seeking treatment were embarrassment, loss of daily wages, and the thought that it would heal by itself. The majority of those who took treatment went to traditional healers, and a Papanicolaou smear was not conducted on any patient[7]. Awareness and practice of the screening for cervical cancer was very poor in the rural population as well as in health care providers. Hence intensive health education is the need of the hour to change the scenario[27].

Incidence and Mortality Rates :

The incidence and mortality rates of cervical cancer in the world are 13.1/105 and 6.9/105, respectively. In India[17]. Overall, from 1990 to 2019 Jharkhand (Incidence: -50.22%; Mortality: -56.16%) recorded the highest percentage decrement in cervical cancer incidence and mortality followed by the Himachal Pradesh (Incidence: -48.34%; Mortality: -53.37%). Tamilnadu (1st rank), Jammu & Kashmir and Ladakh (32nd rank) maintained the same rank over the period of three decade for age standardized cervical cancer incidence and mortality. The regression model showed a significant declining trend in India between 1990 and 2019 for age standardized incidence rate (AAPC: –0.82; 95%CI: –1.39 to –0.25; $p < 0.05$) with highest decline in the period 1998-2005 (AAPC: –3.22; 95%CI: –3.83 to –2.59; $p < 0.05$). Similarly, a significant declining trend was observed in the age standardized mortality rate of India between 1990 and 2019(AAPC: –1.35; 95%CI: –1.96 to –0.75; $p < 0.05$) with highest decline in the period 1998-2005 (AAPC: –3.52; 95%CI: –4.17 to –2.86; $p < 0.05$)[26]. The global scale-up of HPV vaccination and HPV-based screening—including self-sampling—has potential to make cervical cancer a rare disease in the decades to come[24].

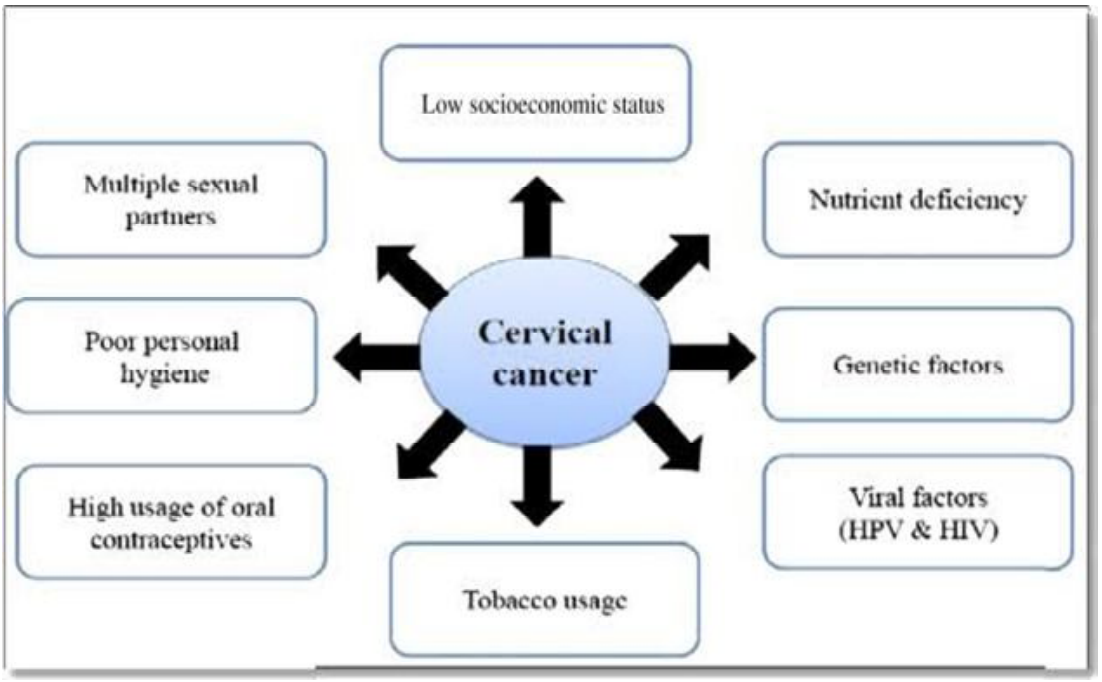
Risk factors in the Indian population :

Cancer with education, place of residence, using an old cloth sanitary napkins,

young age at marriage, number of husband's partners, washing the genitalia after sexual intercourse, and availability of health services. Bathing daily and during menstruations was found to be preventive factors for cervical cancer[30], the association between early age at first coitus and cervical cancer in women with a low rate of sexual promiscuity and define the role of these risk factors in cervical carcinogenesis among rural Indian women[22]. HPV as a direct cause of cervical cancer suggesting urgent need of screening programs and HPV vaccination in women with low socio-economic status and those residing in rural areas[45]. India shows some of the highest rates of cervical cancer worldwide, and more than 70% of the population is living in rural villages[37]. There was a significant association ($P < 0.05$) of cervical

Preventive strategies :

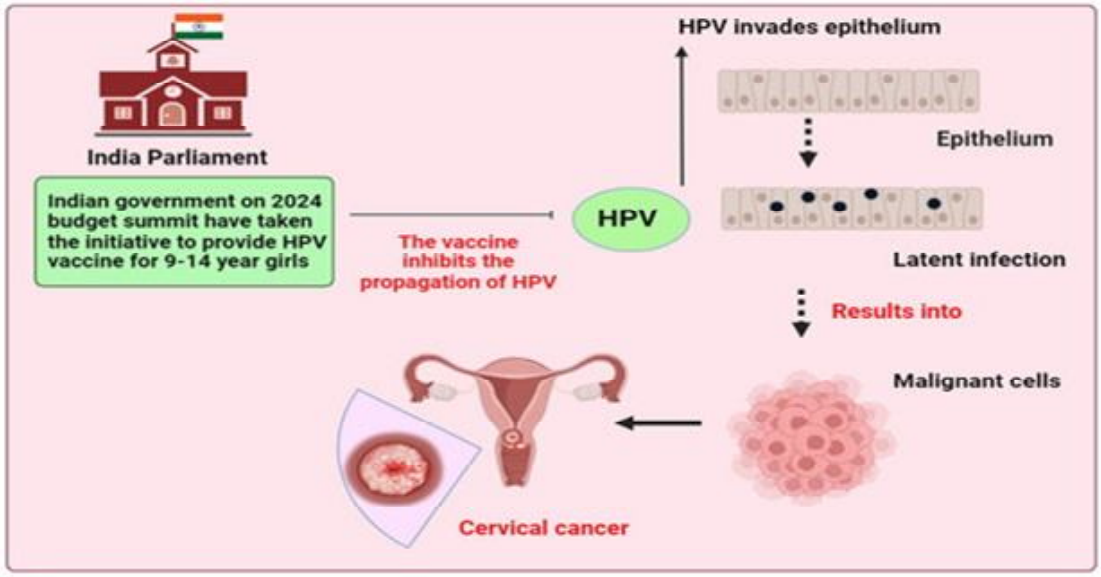
The cost effectiveness of various screening strategies for cervical cancer and human papilloma virus (HPV) vaccination in India is based on Markov model on societal perspective was designed to estimate the lifetime costs and consequences of screening (with either visual inspect with acetic acid (VIA), Papanicolaou test or HPV DNA test at various time intervals) in a hypothetical cohort of 30–65 years age women or vaccination among adolescent girls[2]. Despite being a preventable disease, cervical cancer claims the lives of almost half a million women worldwide each year. India bears one-fifth of the global burden of the disease, with approximately 130,000 new cases a year cervical cancer prevention and treatment services in Uttar Pradesh, a strategic assessment was conducted



and there were gaps in provider knowledge and practices to address gaps in services and unmet needs, state policies and integrated interventions have the potential to improve the quality of services for prevention of cervical cancer in Uttar Pradesh[39].

Vaccination program :

Efforts are being made to scale up human papillomavirus (HPV) vaccination for adolescent girls in India. Bivalent and quadrivalent HPV vaccines were licensed in the country in 2008 and a nonavalent vaccine was licensed in 2018 [41]. The Indian Academy of Pediatrics Committee on Immunization (IAPCOI) recommends offering HPV vaccine to all females who can afford the vaccine. Vaccination can be given to females as young as 9 years as well as in those aged 13–26 years who have not previously completed vaccination. The primary obstacle to HPV vaccination is financial[46]. The development of an affordable, point-of-care HPV test is urgently needed to facilitate its introduction in low- and middle-income family. HPV vaccination efforts need to be speeded up[31]. Prevention of cervical cancers with two-dose HPV vaccination and early detection of precancerous cervical lesions of the eligible population through screening and their appropriate treatment with a single-visit 'screen-and-treat' approach appear to be promising for low-middle-income countries including India[19]. Over the last few years millions of doses of the HPV vaccine have been administered round the world and the efficacy and safety data have started coming from the real life programs[34]. Although widespread and organized screening programs can facilitate earlier detection and management of precancers and cancers, thereby leading to decreased mortality, such screening programs are logistically highly complex, resource intensive, and at a nascent stage in India. Less than 5% of the eligible women in India have ever been screened[40].



Screening and early detection method :

Several screening methods, both traditional and newer technologies, are available to screen women for cervical precancers and cancers[18]. Four types of visual detection approaches for cervical neoplasia are investigated in India: a) naked eye inspection without acetic acid application, widely known as 'downstaging'; b) naked eye inspection after application of 3-5% acetic acid (VIA); c) VIA using magnification devices (VIAM); d) visual inspection after the application of Lugol's iodine (VILI)[36]. Different screening strategies such as rural cancer registries and camp approach for cancer detection have been found useful in minimizing the problem of cervical cancer in the villages[5]. Visual screening test such as VIA/VILI should be adopted as an integral part of primary health-care setup in resource-poor countries like India[43]. The combined estimates of sensitivity for visual inspection with acetic acid, magnified visual inspection with acetic acid, VILI, Hybrid Capture 2 assay, conventional Papanicolaou smear, and LBC were 77%, 64%, 91%, 74%, 59%, and 88%, respectively; the combined values of specificity of these screening strategies were 87%, 86%, 85%, 92%, 94%, and 88% [10]. The sensitivity of visual inspection by paramedical workers to detect cervical cancer was 90.0% using the low threshold and 60.0% with the high threshold to define a positive test[25].

Barriers to accessing healthcare services :

Rate of compliance to cervical screening in Indian population is rare[49]. Programs by focusing on aspects of accessibility, affordability[35]. Due to late presentation to doctors, there is a lower cure rate Rural women's revealed how embarrassment and fear of screening and cultural factors such as lack of spousal or family support could be obstacles to screening[6]. Large amount of lack in awareness and perception in Indian women. Surprisingly all women presented were married. Only 9.59% of women had ever heard of cervical cancer[42]. Ethnic minority women are less likely to attend cervical screening[21]. The Government's investment in health is 0.9% of the GDP. Thus cytology screening as a government health measure is not feasible[13].

Surgery :

Surgery plays an important role in the management of early-stage cervical cancer. Type III radical hysterectomy with bilateral pelvic lymph node dissection using open route is the standard surgical procedure[33]. Treatment of cervical cancer by surgery or radiotherapy results in permanent infertility which affects the quality of life of cancer survivors[32]. Health system cost for different cervical cancer treatment modalities ie radiotherapy, brachy-therapy, chemotherapy and surgery, ranges from INR 19,494 to 41,388 [23].

Chemotherapy and Radiotherapy :

Management of cervical cancer has undergone refinement in the past two decades; concurrent chemo-radiation (CCRT) (with cisplatin alone or in combination) is currently the standard treatment approach for patients[20]. Eligible patients were between 18 and 65 years old and had stage IB2, IIA, or IIB squamous cervical cancer[48]. Treatment in patients of

advanced cancer cervix by neo-adjuvant chemotherapy (NACT) followed by External Beam Radiotherapy (ERT) and Brachytherapy (BT)[16]. Standard management for locally advanced squamous cell cervical cancer is radiotherapy[12].

Clinical trials and emerging therapies :

Cervical cancer is the leading gynecologic health problem the clinical trial on pipeline drugs leads to the development of some promising new therapies the pharmacokinetic/ pharmacodynamics aspects of various pipeline drugs that are promising for the treatment of cervical cancer[47]. Concurrent cisplatin with radiation and lately, gemcitabine-cisplatin chemoradiation has resulted in small but significant improvements in the treatment of locally advanced and high-risk early-stage patients[3]. Cervical cancer is persistent infection with high-risk subtypes of the human papillomavirus and the E5, E6 and E7 viral oncoproteins cooperate with host factors to induce and maintain the malignant phenotype[8]. Two studies are ongoing to optimize treatment after radical hysterectomy. These studies compare chemoradiation versus radiation in intermediate-risk patients or increasing treatment intensity (chemoradiation plus adjuvant chemotherapy versus chemoradiation) for high-risk and locally advanced cervical cancer[4]. Palliative chemotherapy continues to be the standard of care for patients who are not contenders for curative therapies like surgery and radiotherapy[38]. Molecular aberrations in cervical cancer and new therapeutic modalities are emerging, including immune checkpoint inhibitors, therapeutic vaccines, antibody-drug conjugates, and others[9]. Immune landscape of cervical cancer and the growing clinical data regarding the use of immunotherapy[28].

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