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A Study of Detection of Cervical Cancer Using Immunotherapy of Women in India

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Abstract:

The prevalence of women in India who get cervical cancer has gone down, but it is still a big public health issue for them. In light of cervical cancer's many causes, many ways to prevent it, and huge risk, more research is needed. Here, we talk about things like the prevalence and pattern of cervical cancer, HPV (human papilloma virus) types that are common in both cervical cancer patients and women in general, high-risk groups like commercial sex workers and HIV-positive women, and more. In women who are 55 to 59, this disease is most common. Many of them are found at a late stage.

Keywords: HPV, cervical cancer, prevention, screening, epidemiology.

1. Introduction

The most common type of cervical cancer that kills people in poor countries is the most common type of cancer in the United States. Because 86 percent of cervical cancer deaths happen in developing, low- and middle-income countries, cervical cancer mortality is a good way to see how different countries are when it comes to health. There are about 122,844 cases of cervical cancer in India each year, and 67,477 women die from it. There are 432.2 million Indian women over the age of 15 who are more likely to get cancer. As a cancer, women between the ages of 15 and 44 are most likely to get breast cancer. People in India have more cervical cancer than Bangladesh has (19.2), Sri Lanka has 13, and Iran has 11. (2.8). In India, more needs to be known about cervical cancer's spread.

When India's national cancer control program first started in 1984-1985, the main goal was to equip top-tier cancer institutes. By 1990-1991, the main goal had changed to primary cancer prevention and early detection, and district cancer control programs had taken over from them. New regional cancer centers were a top priority for the program in 2008. The program also aimed to strengthen current regional cancer centers, build new ones, and expand oncology wings in medical college hospitals.

There are big differences in how people are screened, how they are treated, and how long they live because there is no national screening program. According to a population-based survey analysis of surveys, coverage of cervical cancer screening in developing countries ranges from 1% to 73.33%. This is not the case in rich countries. Cancer-related deaths are highest in women over 50 and those who are poor, but they are the least likely to be screened for it. There was a wide range of screening rates in India's different states, from 6.9% in Kerala to 0.06 in Maharashtra and 0.002 in Tamil Nadu and Kerala. 85% of the patients have already reached an advanced or terminal stage, and more than half of them (63%) have already had regional illness when they first come to the hospital. Detecting and treating cervical cancer in its advanced stages costs a lot, and poor prognosis makes people less likely to follow through with treatment. During 1992 and 1994, a Mumbai population-based cancer registry found that the five-year survival rate for cervical cancer was 47%, which is about half. The length of a woman's life was affected by how old she was and how bad her illness was. People who live in Bangalore for five years have a survival rate of 34.4% and a relative survival rate of 38.3% from the 1980s. From 1982 to 1989, the registry saw a big drop in the number of people who came in with Stage IV cancer. This shows that people's knowledge of the disease has gone up.

1.1 Cervical Cancer Epidemiology in India

In the last two decades, cervical cancer has been the most common malignancy among women. Cervical cancer incidence is highest in India between the ages of 55 and 59. Breast and cervix cancer are the most frequent cancers in women, according to data from the National Cancer Registry Program (NCRP). According to the most recent NCRP statistics, between 2009 and 2011, Aizawl district in north-eastern India had the highest age-adjusted rate of cervical cancer, followed by Barshi. According to data collected between 2009 and 2011, Bangalore grew to 19.5 and contracted to 18.9 according to data collected between 2009 and 2011.Age-adjusted mortality rates dropped from 32.4 in 1982 in Bangalore to 18.7 in 2009 in Barshi, from 22.1 in 1988 to 14.1 in 2010, from 41 in Chennai to 16.7 in 2009, and from 9.2 in 2005 to 7.7 in 2011 in Thiruvananthapuram. Between 1982 and 2010, the annual percentage decline ranged from a low of 1.3 percent in Bhopal to a high of 3.5 percent in Chennai. Age-adjusted mortality rates in all of the older PBCRs fell significantly between the 25–34 age bracket and 54, although the Barshi registry only

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showed a drop up to 44 years. The cervical cancer incidence rates are shown in Figure 1 for the year 2010. Squamous cell carcinoma is the most prevalent histological type in the ectocervix, and adenocarcinoma is the most common in the endocervix.

It's clear that the age-adjusted mortality rate has been steadily decreasing even without a control programme. The Bangalore Cancer Registry has been showing a downward trend since 1995. According to NCRP, the mortality statistics for cervical cancer are insufficient as the reason of death is often missing. All incident data has been thoroughly vetted for accuracy and completeness. Hospital-based cancer registries give information as a result of a complicated interaction between illness incidence and health care-seeking behaviour, which is best reflected in population-based cancer registries. Hospital-based registries have shown a significant increase in both breast cancer and cervical cancer over the course of 30 years in the Mumbai registry (95 percent confidence interval: 2.0, 1.6).

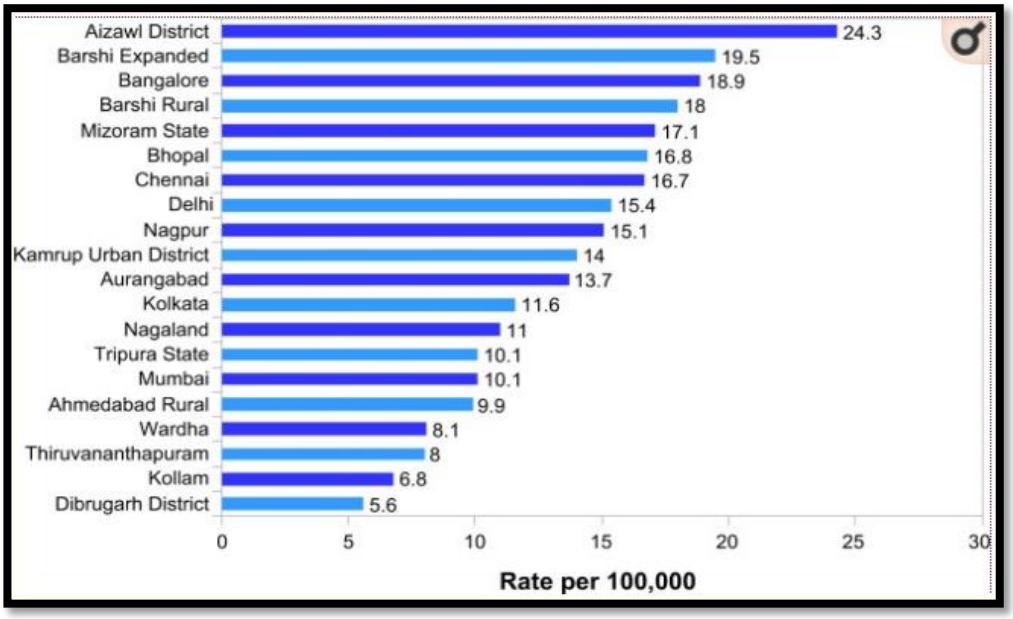

Figure 1 Age adjusted incidence rates of cervix uteri-females (rate per 100,000) in the various population based cancer registries

1.2 Using the immune system to treat cervical cancer

HPV infection can be controlled by the immune system. The course of disease in HPV-induced carcinogenesis will be determined by alterations in the microenvironment and the interaction between virally-infected keratinocytes and the local immune milieu. Antitumor immunity may be released or generated through immunotherapy strategies that rebalance the local immune components, allowing existing or new antitumor immunity to be released. In order to eradicate cancer, the immune system can be employed to identify and target virus-associated tumour cells, or to release CTLs from their negative feedback loop, allowing them to attack cancerous cells.

1.3 Vaccines for therapeutic purposes

By using constitutively expressed tumor-specific antigens E6 and E7, therapeutic vaccines activate and promote the development of T lymphocytes that specifically detect and kill cancer cells. At least one antigen-presenting cell (APC) must be activated by the antigen before any protective immune response may be induced. Cervical cancer vaccines have been developed with various strengths and weaknesses, immunogenicity and efficacy in mind for the treatment of HPV-related diseases. Live-vector vaccines can elicit strong immune responses, both cellular and humoral, because of their high immunogenicity. An APC is stimulated to display antigens by delivering E6 and E7 antigens through the major histocompatibility complex (MHC) classes I and II in these vaccinations. This method has a few drawbacks, including the danger of injury to immunocompromised patients and the inability of the immune system to respond well to repeated vaccinations with the same vector. Listeria monocytogenes (Lm) is used as a bacterial vector in the development of ADXS11–001, commonly known as AXALTM (Advaxis). When the Lm bacteria enters a host cell, it can infect and activate both the immune system's innate as well as adaptive responses. In the ADXS11-001 live attenuated L. monocytogenes vaccine (LLO), the HPV-16 E7 antigen is fused to a non-hemolytic fragment of the Lm

protein listeriolysinO. In contrast to conventional immunotherapies, which produce neutralising antibodies, Lm-LLO treatments promote chemotaxis of activated immune cells and stimulate strong immunological memory.

1.4 Inhibitors to the checkpoint

Antitumor immune cells are activated when checkpoint inhibitors deactivate inhibitory receptors on immune system elements. It is hypothesised that virus-induced malignancies will respond differently to immune checkpoint inhibitors than other tumours. A larger mutational burden may lead to a better response, resulting in a differential cancer response. PD-L1 expression as a biomarker of response in virus-induced malignancies is controversial due to the lack of clarity regarding the suitable cut-off values measuring clinically significant PD-L1 expression44 and the lack of data indicating association with treatment results in cervical cancer patients. The fact that invading TILs express higher levels of PD-1 suggests that blocking PD-1/PD-L1 may have therapeutic value in patients with cervical cancer. Anti-PD-1 and anti-PD-L1 therapies. The immunological regulatory axis of the programmed cell death protein1/programmed death ligand-1 is a viable target for the treatment of cervical cancer. This antibody, manufactured by Merck Sharp & Dohme, is an IgG4 kappa monoclonal immunoglobulin G4 (IgG4) anti-PD-1 monoclonal antibody for the treatment of patients with advanced cancer. PDL1-positive (1%) advanced solid tumours including cervical cancer were included in the expansion cohort of the phase Ib KEYNOTE 028 research, which included 24 patients with metastatic or unresectable CSC who had previously failed systemic treatment.

1.5 Antigen 4 of cytotoxic T-lymphocytes

This receptor was the first to be targeted therapeutically. Immune system overactivity can be prevented by downregulating the function of T cells, which are only found on T cells. Patients with metastatic or recurrent cervical cancer received the drug ipilimumab (Bristol-Myers Squibb) in a phase I/II trial. In 42 patients, the median PFS was 2.5 months (95 percent CI: 2.3–3.2), with grade 3 toxicities including diarrhoea and colitis. Ipilimumab is being studied in a phase I clinical trial in patients with node-positive cervical cancer who have had chemotherapy and radiation therapy. 34 women with cervical cancer in FIGO stages IB2/IIA or IIB/IIIB/IVA and positive lymph nodes participated in the trial.

1.6 Adoptive cell transfer to treat disease.

After ex vivo amplification and with or without genetic alteration, adoptive transfer of tumour-antigen targeting T lymphocytes into a cancer patient is a viable therapy method. However, its drawbacks are the difficulty of the technology, the high intensity of the labour, and the expensive cost. Ex vivo tumour specimen culture and lymphocyte growth as part of adoptive T-cell therapy (TILs). When a specific type of antigen and phenotype of T cells are discovered in vitro, they can be grown and expanded. These T cells are injected into individuals who have undergone lymphodepleting chemotherapy and have autologous tumours.

Naresh Poondla (2021) Squamous cell carcinomas account for 70–80% of all cervical cancers, while adenocarcinomas account for 10–15% of all cervical cancers. According to HPV infection rates, roughly 90% of all instances of cervical cancer are linked to the virus. Smoking, a weakened immune system, the use of birth control pills, the onset of sexual activity at a young age, and a large number of sexual partners all increase the chance of HIV infection. It's also worth noting that CC is one of the rare tumours that can be entirely avoided. If caught early enough or prevented through healthy practises like safe sex, routine screening, and vaccination, it can be reversed or totally healed. To be sure, modern medical improvements have made early detection possible through low-cost, self-sampling methods, which have greatly lowered mortality, but incidence rates, particularly in older women, have not declined significantly. Government and non-government organisations have committed to and are taking steps to safeguard girls and women from CC through screening and vaccination. By raising awareness of the importance of early detection and treatment, we can not only eliminate cervical cancer but also protect the reproductive health of women. As a result, the purpose of this review is to educate the public about CC by providing an update on the most recent medicinal advancements, while also establishing the basics of CC, such as its causes, types of treatment methods, advanced treatment modes, opportunities for prevention, the most recent technology (including clinical trials), and financial situation for the treatment of this deadly disease.

Saurabh Bobdey (2016), more than a quarter of the worldwide burden of cervical cancer mortality is borne by poor countries. Despite the disturbingly high numbers, no government-sponsored screening programme exists in India. According to this study, India's cervical cancer burden and the performance characteristics of current screening techniques were reviewed in order to provide evidence-based recommendations for the usage of the most feasible screening test in resource-poor settings.

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Asmita Pal (2020) Cervical cancer caused by the human papillomavirus (HPV) is a severe problem for women in developing countries. Late diagnosis and poor prognosis contribute to a high death rate. Two main oncogenes, E6 and E7, which are expressed constitutively and lead to carcinogenesis, are fully necessary for the onset and subsequent advancement of this type of cancer. As a result, the most effective method of treating cervical cancer involves genetic alteration. In this article, E6 and E7 activity have been examined in terms of structural, functional, and clinical aspects. All of E6 and E7 protein structure and genomic organisation, as well as the process by which they produce the six primary cancer hallmarks in cervical tissues for tumour proliferation, have all been examined in depth. The next section of this review article focuses on the several types of therapies that work by deregulating the activity of E6 and E7. It has been proven time and time again that therapeutic techniques that target E6, E7, and other indicators of cervical cancer cell proliferation are particularly effective in removing abnormally proliferating malignant cells. Cervical cancer cells infected with HPV have been successfully reduced by therapeutics comprising vaccinations and genome editing approaches that limit E6 and E7 activity. Another promising treatment option to destroy HPV-infected tumorigenic cells is T-cell immunotherapy. As a result of this study of phytotherapeutic techniques, anticancer properties of natural chemicals derived from plants or other natural repositories have been demonstrated. In this study, we provide an in-depth look at the signalling pathways and molecular mechanisms by which E6 and E7 suppress cervical cancer growth through a variety of techniques.

2. RESEARCH METHODOLOGY

The majority of cervical cancer deaths occur in third world countries. An important principle in the treatment of this health issue is prevention. Tests like the PAP smear easily detect this. While it is true that precancerous cells identified and removed, we can't roll out a countrywide campaign against cervical cancer application for screening. Roughly eighty-five percent of all cases of Cervical cancer at its advanced stages. With time, the prognosis worsens with each passing step. Moreover, the administration of cost prohibitive in the more developed stages. This research conduct to learn the causes of people's procrastination in getting help assist in the medical field. A cross-sectional study was conducted from January 2015 to December 2016.

- **Criteria for inclusion**

  The study included patients in the outpatient gynaecology and radiotherapy departments who had histologically confirmed stage 2b or higher cervical cancer.

- **Exclusionary factors**

  The study did not include women with cervical cancer that was less than stage 2b. There were a total of 100 ladies that participated in the study. The patient was required to sign a consent form after being fully briefed. A questionnaire was created to gather all of the essential data. The institution's ethical committee gave the go-ahead.

  For each question in the questionnaire, the percentage of respondents who answered it was determined using a basic grid.

3. RESULTS AND DISCUSSION

One hundred women with a stage above cervical cancer were asked about their health. Most of the patients were over the age of 40, from poor families, and from rural areas, but not all of them. Every one of them was a mother. Most women have at least four or more problems in their lives at any given time. A lot of people (61%) said they had irregular bleeding, followed by discharge PV (41%) and post-coital bleeding (3%). (22 percent). A lot of people who had been having problems for five to ten years didn't go to the doctor, and almost a third didn't tell their family about their problems. One in three women hasn't seen their doctor in five years. One-sixth of the people who came in had been married by the time they were 18.

Table 1. Demographic profile of women with advanced carcinoma cervix.

Demographic profile	Number of patients (n=100)
Age (years)	

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< 40	15
40-60	44
>60	41
Education status	
Illiterate	88
Primary school passed	12
Age at marriage (years)	
<18	68
>18	32
Parity	
≤2	8
3	22
≥4	70

Most of the patients had never used any kind of contraception in their lives, and none of them knew how it could help them stay healthy. Some 52% were in the clinical stage at the time of diagnosis, while the other 48% were in a more advanced stage. Over the counter medicines were used by about 80% of patients who didn't see a doctor about their health problems. Many people (98%) didn't know that PAP smears are important for screening for cervical cancer, and nearly all (94%) had never had a PAP smear test. Almost 3% of people had a family history of the disease, but no one had ever heard about the symptoms of the disease. None of them knew that the vaccine could help fight cancer. Each and every one of the patients said that if they had known about cervical cancer, they would have come to the doctor sooner.

4. Conclusion

According to this research, the most common reason for a delayed response is a lack of understanding of the disease. This group of high-risk women for cervix cancer should be targeted and taught through the media so that they can seek treatment at an early stage while the author works to implement a national screening programme. Many immunotherapy techniques are now being evaluated in order to treat high-risk, locally progressed, and recurrent or metastatic cervical cancers. Phase I and II clinical trials show promising results, but the best timing for delivering immunotherapy methods is still uncertain and specific predictive biomarkers are lacking. To prevent cervical cancer, screening programmes, sex education, and treatment of pre-malignant lesions should be prioritised. The majority of women who are diagnosed with this cancer reside in countries where health care is underfunded and tailored therapies are not readily available to those who need them. Patients and their supporters, as well as pharmaceutical corporations, health authorities, and the larger scientific community, must work together to ensure that innovative therapies are more widely available in low- and middle-income nations. This article does not cover the topic of vaccines to prevent HPV infection. Cervical cancer can be eliminated with this method. When a case of cervical cancer arises, our attention should be drawn to methods for reducing the risk of recurrence. Radiation and chemotherapy are being used in conjunction with checkpoint inhibitors or therapeutic vaccinations in this study. Results from phase III randomised trials are awaited before drawing any firm conclusions about metastatic or relapsed illness. If you want to study adoptive cell therapy, for example, you'll need to look into it more. Because these therapies are so complicated, they can only be used in special places for now.

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