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RESEARCH ARTICLE

CERVICAL CANCER IN BIHAR: AN EXPLORATION OF OPPORTUNITIES AND CHALLENGES

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ABSTRACT

Cervical cancer has a major impact on the lives of Indian women with an estimated 132,000 new cases and 67,000 deaths reported worldwide in 2012. Locally advanced cervical cancer is commonly seen in Bihar because of the high prevalence of associated risk factors like low socioeconomic status, poor access to health care, high parity, early age of marriage and first pregnancy, smoking, persistence of genital infection specially HPV, low immune status, poor genital hygiene and nutritional status. Besides, there is lack of organized screening programme and treatment facilities for these patients in Bihar. With this background, this review was done to evaluate data from National census and Health survey in context to the above known risk factors for cervical cancer and methods for improving prevention and treatment of cervical cancer in the state of Bihar. Data from National census of India, 2011 and health survey 2011-12 was evaluated for the prevalence of risk factors in the state of Bihar. Further availability of cancer treatment facilities in the state was also evaluated in terms of requirement as per given standard recommendations.

Conclusion: Increasing awareness about early signs and symptoms especially among the rural population, widespread use of HPV vaccination and simple screening techniques like visual inspection with use of acetic acid is urgently required to control the rising number of cervical cancer cases in the state of Bihar. A tremendous boost is also required in the availability of radiotherapy units, other infrastructure and trained personnel in the field of oncology.

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INTRODUCTION

Cervical cancer has a major impact on the lives of Indian women with an estimated 132,000 new cases of cervical cancer per year. About 80% of these cases present in a locally advanced stage which leads to high morbidity and mortality (Ferlay *et al*., 2013). Because of lack of public awareness and infrastructure for screening and early detection, this late presentation is likely to continue in coming years. Traditionally, risk factors found to be associated with cervical cancer includes low socioeconomic status, poor access to health care, high parity, early age of marriage and first pregnancy, smoking, persistence of genital infection specially HPV, low immune status, and other factors such as poor genital hygiene and low nutritional status (Burd, 2003; Irimie *et al*., 2011; Herrero *et al*., 1990; Mhaske *et al*., 2011; Howkins, 1999; Dutta *et al*., 1990). Cervical cancer is very commonly seen among the female population of Bihar, as is reflected by the large number of these patients coming not only to the cancer hospitals of Bihar, but also to cancer centers situated in big cities of India like Delhi, Kolkata and Mumbai.

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Such a high prevalence of cervical cancer could be related to the presence of the abovementioned risk factors in our state of Bihar. The state of Bihar is one of the less economically developed state of India. About 89% of its total population lives in villages. Agriculture is the main source of income for these villagers and many of them work on daily wage basis on other people's farm. The per capita income for majority of the people in the villages of Bihar is less than the national average. (Directorate of Economics & Statistics of respective State Governments, 2014) Poverty forces them and their family members to live in small congested homes and to eat food which is not very nutritious or healthy. So, they have low immunity and are more prone to develop chronic infections. Further, female children of such household are often not send to school and are married off at an early age. Then they bear children at a young age and usually have multiple pregnancies. Exposure to sexual practice and infection during adolescence, when the transition zone of the cervix is very susceptible to initiation of malignancy is an important risk factor for cervical cancer (Louie *et al*., 2009; Munoz *et al*., 2002; El-Moselhy *et al*., 2016). Tobacco smoking, which is another risk factor for the development of cervical cancer is also seen in many of the female population in the form of bidi smoking (Sinha, 2003).

The use of tobacco could be a co factor for the development of cancer in these people. Besides, the female population living in villages usually have no idea about the early signs and symptoms of malignant diseases due to lack of education and awareness. Further, they have a limited access to even primary healthcare facilities, which often force them to use traditional homemade remedies or alternative therapy which are easily available and affordable for problems like vaginal discharge or abnormal vaginal bleeding. They are also quite hesitant to discuss their gynecological problems with the other male members of the family, who could take them to nearby hospitals for treatment. This results in inadequate treatment of vaginal infections leading to their persistence, which may progress to invasive cervical cancer (Saha *et al*., 2010; Pillay, 2002). Another problem with the cervical cancer patients of Bihar is the late stage at presentation. Low literacy rate, lack of awareness, accessible health care facility and trained oncological personnel are the factors responsible for the late presentation (Tripathi *et al*., 2014). With this background, this review was done to evaluate the published data from National census and Health survey in context to the above known risk factors for cervical cancer, in terms of socio-economic status, literacy, place of living, lifestyle, age of marriage, parity and, availability of cancer treatment facilities among the female population of Bihar. Additionally, brief implications of these factors with their role in carcinogenesis and methods for improving prevention and treatment of cervical cancer will be discussed.

DISCUSSION

For Indian women, cervical cancer is the second most common incident cancer with 1,32,000 new cases and about 67,000 deaths reported in 2012. (Ferlay *et al.*, 2013). Delayed diagnoses and inadequate, incorrect, or suboptimum treatment are the chief factors responsible for poor cancer survival in India (Sankaranarayanan *et al*., 2010). Though alarming, these estimates have several limitations as they represent data mostly from few urban hospitals based cancer registry program. A number of cancer cases and deaths, especially among female and older people usually go unreported in our country because of a number of social and economic factors. It has been observed that the risk of developing cervical cancer is high for most women in the third world due to peculiar socio-economic characteristics including poverty, illiteracy and living in villages. Poverty is a complex issue which includes elements such as unemployment, low levels or no formal education, nutritional deficiencies and living in unhygienic conditions. This group of population have a lot of social disadvantage including ignorance about early symptoms of the disease, lack of awareness of available prophylactic measures, low immunity level, limited accessibility to standard health care and so, they usually present with an advanced stage of cancer (El-Moselhy, 2016). Thus, we see that cervical cancer is a disease of rural population that is closely related to poverty which is a big social issue in our state as per data from the national census.

According to the National Census 2011, Bihar is the third most populated state of India with a population of 10.41 Crores, which forms 8.60 percent of India's total population. The total number female population has been reported to be 49,821,295. Out of these 10.5 crores people, only 11.29% live in urban regions.

An estimated 44,267,586 of females live in the rural areas of Bihar, who have a high risk of developing cervical cancer. Further, the literacy rate in Bihar is 61.80%, which drops down to 51.50% for the female population. Average Literacy rate in Bihar for Urban regions was reported to be 76.86% in which males were 82.56% literate while female literacy stood at 61.95% whereas for rural population, overall literacy rate was 59.78% with 69.67% literate males and only 44.30% literate females (Census of India, 2011). The cause for this low literacy rate could be the high prevalence of poverty seen in our state. Bihar has a per capita income of $360 a year against India's average of $1265 and 30.6% of the state's population lives below the poverty line against India's average of 22.15%. (Directorate of Economics & Statistics of respective State Governments, 2014) The level of urbanization (10.5%) is below the national average (27.78%). Even urban poverty in Bihar (32.91%) is above the national average of 23.62% (Census of India, 2011)

Illiteracy and poverty further leads to marriage of girls at an early age, multiparity and gender inequality as the health issues of the females is not taken seriously by the family members. The facts from the latest National census and health survey shows that the above issues are highly prevalent in Bihar. As per annual health survey 2011-2012 fact sheet, marriages below the legal age of 18 years was reported among 17.8% of rural population as compared to 8.4% among urban female population of Bihar during 2008 to 2010. Currently, women in the age group of 20 to 24 years who were married before the age of 18 years was found to be 53.5% among rural population as compared to 42.40% among urban females. They reported the mean age of girls at marriage to be 19.9 years among rural population and 21.6years among urban population of Bihar. The median age at first live child birth was 21.5 years and 22.4 years among rural and urban women of the state respectively. A survey of the women revealed that on an average 47.7% of them were either pregnant or already mother at the age of 15 to 19 years (Annual Health Survey, 2011-12).

Studies have proven that the presence of human papilloma virus (HPV) which is contracted via sexual intercourse is the most important causative factor for the development of cervical cancer (Burd, 2003; Munoz *et al*., 2002) Various studies in the developing world have established that early marriage leading to early age at first intercourse and early age at first pregnancy are risk factors for cervical cancer, irrespective of other known risk factors for the disease (Louie *et al*., 2009). The mechanism by which the early age of first sexual intercourse and first pregnancy could influence the risk of cervical carcinogenesis may be explained by the steroid hormonal influence on HPV infection and on the host's immune response to HPV during pre-adolescence and adolescence (Elson *et al*., 2006; Giannini *et al*., 1998). The transformation zone of the cervical epithelium is the site at which HPV infection tends to initiate cancer, and the susceptibility of this area is believed to be related to the denudation of its stratified epithelium, thus facilitating exposure of the basal layer to HPV with minimal trauma (Munoz *et al*., 2002) Biological immaturity during adolescence has also been proposed as an additional susceptibility factor. During adolescence and pregnancy, the cervix is exposed to augmented levels of hormonal changes in which estrogen stimulation facilitates acidification of the vaginal cavity, a determinant of squamous metaplasia when the endocervical epithelial everts.

When this estrogen-stimulated metaplastic transformation occurs in the presence of HPV, the probability of cell transformation increases, resulting in neoplastic changes. This phenomenon is dependent primarily on parity, and is more likely to occur during the first pregnancy rather than subsequent pregnancies (Hwang *et al*., 2009; Moscicki, 1989). Besides, early age of marriage and early age at first child birth, multiparity is also a common feature seen among the rural population of Bihar. The mean number of children in women in the age group 45 to 49 years was reported to be 5 and 4.3 respectively for rural and urban group respectively. (Annual Health Survey, 2011-12). Multiparity is a marker of repeated cervical trauma and repair which can induce metaplastic changes and so, a strong risk factor for cervical cancer. Further, increased endogenous estrogen level as that seen during pregnancy can lead to persistence of HPV infection. The higher density of estrogen receptors and their expression in the transformation zone may synergize with the effects of HPV oncoproteins, decreasing levels of cytotoxic cytokines that may down-regulate the cervical cell-mediated immune response, causing persistent HPV infections instead of clearance (Munoz *et al*., 2002; Hwang *et al*., 2009). Similarly, poor genital hygiene also leads to persistence of HPV infections and is therefore an important risk factor for cancer especially in a state like Bihar where clean water and other sanitation facilities are limited for majority of the rural population (De Sanjosé *et al*., 1996; Siné Bayo *et al*., 2002).

The per capita water supply in Bihar is 61 litres per day, much below the national average of 142 litres per day. Only 52 percent of rural households in Bihar get their daily supply of water throughout the year from piped water at home or public tap/standpipe (both for drinking and other household use). With no bathing facility for 66% of poor women and girls in rural areas of Bihar, their personal hygiene practices are adversely affected (Census of India, 2011) Some studies have shown that women are also at risk of exposure to reproductive tract infections (RTI), urinary tract infections (UTI), and Human papilloma virus (HPV infection which causes cervical cancer) due to poor water, sanitation and hygiene conditions and inability to afford sanitary material for menstrual protection (Kumar, 2013). In communities where women have to haul water from long distances, defecate in the open, and bathe in public fully clothed not only do women bathe infrequently, they are unable to maintain vulvar and perineal hygiene on a daily basis increasing the risk of various infections including HPV (Rita Jalali, 2014).

In addition to the presence of the above mentioned potential risk factors for the development of cervical cancer, there is lack of an organized screening programme and treatment facilities for cervical cancer patients in Bihar. Curative treatment for cervical cancer requires surgery, radiation (both external beam radiotherapy and brachytherapy), chemotherapy either alone or in combination (NCCN Guidelines, 2015) As more than 80% of the cervical cancer patients present in an advanced stage, radiotherapy along with chemotherapy is the single most important treatment modality required for our patients. This standard treatment requires the patient to stay near the cancer hospital for about two months as they have to come daily for the radiation therapy. As per the guidelines by the International Union Against Cancer, one cobalt or radiotherapy unit is required for treatment of cancer patients for one million populations in the developing countries (Gupta, 2006).

Based on this recommendation, the actual requirement of radiation unit required works out to be 117 for the population (Murthy *et al.,* 2016) of Bihar. However, the current radiotherapy facilities in Bihar is very less than that required; with the availability of only 6 teletherapy (2 Linear Accelerator and 4 $Cobalt^{60}$ machine) and only 2 functional brachytherapy units for the entire population of Bihar. Other factors such as the preferences of doctors for working in urban areas and a largely unregularized private practice have further skewed the geographical distribution of cancer treatment facilities. Out of 38 districts in Bihar, all the radiotherapy units and most of the trained oncologists are available only in Patna, the capital city of Bihar and so, most of our patients have to travel long distances for the treatment. This further worsens the situation for women, the frail, the elderly, and those with low incomes who are unlikely to have the resources and support they need to travel comfortably to these cancer centers. This distance barrier forces a number of poor patients living in remote villages to die with the disease without any standard treatment, which might have otherwise cured them. Even after these patients manage to reach treatment centers, they typically have to stay in what are often over-crowded and unhygienic dharmshalas or private lodging houses for a long period of 6 to 8 weeks, which is the time required for the completion of radiotherapy treatment which further poses additional financial burden to the cancer patients. Many are therefore exposed to the risk of contracting infections, and so might be unable to complete treatment regimens in a timely way. This could well be one of the factors that contributes to our disproportionately high cancer incidence-to-mortality ratios, alongside late diagnosis (Palacio-Mejía, 2003).

The existing treatment facilities for cancer control in-terms of radiotherapy units are inadequate to take care of even the present load; with an expected increase in the number of patients in coming years because of increasing longevity and rising population (Murthy, 2016). So, mobilization of resources for purchase and instalment of radiotherapy units is another important issue in our context. The high cost of imported radiotherapy equipment and sources are major problems in establishing cancer hospitals. The advent of new machines like linear accelerator which uses conformal techniques to treat cancer further increases the financial burden. In low resource setting like ours, at least Cobalt machine, which is less costly and easy to maintain than the modern linear accelerator machines should be made available at all medical colleges of Bihar. This Cobalt machine can be used to treat effectively most of our patients with results equivalent to modern linear accelerators in less time and with less technical and financial resources. Further, local manufacturing of equipment with cost effective innovative designs is required to reduce the cost of these machines and thereby treatment (Page, 2014)

The current infrastructure for management of cervical cancer burden in Bihar is in sufficient not only in terms of radiotherapy machines, but also in number of trained and qualified oncologists, other allied health personnel including onconurses, and of the training facilities needed to produce them. In Bihar we have only a handful of trained oncologists, medical physicist, radiotherapy technicians and other staff required for comprehensive oncological care. Regarding training facilities in oncology, only 4 DNB seats in radiotherapy and 2 seats in surgical oncology, recognized by National Board of Examination, New Delhi is available in

Bihar. An oncological wing with facilities for oncosurgery, radiotherapy and chemotherapy should be added to each and every medical college of Bihar. The regional cancer centre and the district cancer control program should be strengthened. To tackle the manpower crisis, oncological training programs for doctors and other allied health personnel is required. There should be regular seminars and training workshops to upgrade the knowledge and skill of medical professionals. (Murthy, 2016).

The current review shows a high prevalence of risk factors for cervical cancer in the state of Bihar like poverty, illiteracy, slow pace of urbanization, early age at marriage and first child birth along with multiparity and lack of water and other resources for proper sanitation which is probably responsible for the large burden of cervical cancer present in the state. The high prevalence and mortality rate seen is all the more disappointing; as cervical cancer is one of the most preventable type of cancer (Basu *et al*., 2013). Routine screening and increased awareness has been shown to successfully decrease the prevalence of this disease among the female population of developed countries. An analysis of population-based surveys indicates that coverage of cervical cancer screening in developing countries is 19% compared to 63% in developed countries (Gakidou *et al*., 2009) Moreover, early detection and standard treatment has resulted in 5year survival rate to be more than 90% as seen in developed countries compared to around 30% as seen in developing countries because of late diagnosis and improper or incomplete treatment. Recently, routine use of vaccine against cervical cancer has been incorporated in the national vaccination schedules of many developed countries of the world. This is expected to further decrease the burden of cervical cancer. The main elements in the guidelines on comprehensive cervical cancer control from WHO include vaccination of 9 to 13-year-old girls with two doses of HPV vaccine to prevent infection with the Human papillomavirus (HPV), the virus responsible for most cases of cervical cancer, use of regular screening tests like VIA and HPV tests to screen women for cervical cancer prevention, wide communication for creating awareness and addressing inequities in health care (World Health Organization, 2013).

In a state like ours the problems are further complicated by the fact that we do not even have an accurate estimation of the cervical cancer load present in Bihar. The availability of such data is required for planning of an adequate infrastructure for screening and treatment by the Government or any other authority. So, cancer should be made a notifiable disease as this would help in making precise projections and the proper implementation of cancer control strategies. The best cost effective solution to our problem is prevention, both at primary and secondary level. We need to have a robust screening program, which should be practical and acceptable to our population along with a stress on increasing awareness among the general population of Bihar, especially for women from low socio economic strata as cervical cancer is the disease of low socioeconomic population (Seema, 2003) Cost effective methods of screening through simple visual inspection of cervix, application of acetic acid seems to be more practical for our state, as compared to costly recommended techniques like HPV DNA testing used in developed countries. Cancer awareness programs for school, colleges and general public should be organized at regular intervals. Social workers and NGOs should be encouraged to actively organize such awareness programs.

Primary prevention in the form of vaccination is the real hope for reducing cancer morbidity and mortality in our state. The success of HPV vaccine, Cervarix and Gardasil in developed countries has proved its efficiency in preventing cervical cancer. However, the cost and acceptance of these vaccines in our population is a major hindrance for its use in India. Currently, the two available HPV vaccines in the market are costly and beyond the reach of the poor rural population of Bihar, who is at high risk of developing cervical cancer (Kaarthigeyan, 2016). Like many other countries of the world, Govt. of India should also strengthen its efforts to prevent cervical cancer by introducing HPV vaccine into routine immunization schedule as its use can reduce the chance of developing HPV related cancer by up to 80%. Recently, the Union Government has indicated that it may include HPV vaccines in its National Immunization Program. The inclusion of HPV vaccines in the National Immunization Schedule and its routine use will definitely be one of the biggest step in the prevention of this dreaded disease among our people.

Conclusion

Cervical cancer is still a major cause of morbidity and mortality among our female population. Poverty, illiteracy, ignorance, early age of marriage, early age at first pregnancy, multiparity, lack of screening and treatment facilities are the major contributing factors. Cervical cancer can be prevented with the use of HPV vaccines and proper treatment of precancerous lesions, which can be easily detected by visual inspection and simple cost effective tests like Pap smear examination. Besides prevention, availability of proper infrastructure and an adequate number of trained oncologists for treatment of cervical cancer is also urgently required in our state.

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