RESEARCH ARTICLE

Statistical Modelling and Forecasting of Cervix Cancer Cases in Radiation Oncology Treatment: A Hospital Based Study from Western Nepal

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Abstract

Background: To estimate the numbers and trends in cervix cancer cases visiting the Radiotherapy Department at Manipal Teaching Hospital, Pokhara, Nepal, statistical modelling from retrospective data was applied. Materials and Methods: A retrospective study was carried out on data for a total of 159 patients treated for cervix cancer at Manipal Teaching Hospital, Pokhara, Nepal, between 28th September 2000 and 31st December 2008. Theoretical statistics were used for statistical modelling and forecasting. Results: Using curve fitting method, Linear, Logarithmic, Inverse, Quadratic, Cubic, Compound, Power and Exponential growth models were validated. Including the constant term, none of the models fit the data well. Excluding the constant term, the cubic model demonstrated the best fit, with R^2=0.871 (p=0.004). In 2008, the observed and estimated numbers of cases were same (12). According to our model, 273 patients with cervical cancer are expected to visit the hospital in 2015. Conclusions: Our data predict a significant increase in cervical cancer cases in this region in the near future. This observation suggests the need for more focus and resource allocation on cervical cancer screening and treatment.

Keywords: Statistical modelling - cervix cancer - curve fitting method - Nepal

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Introduction

According to the WHO Report of 2010, cervical cancer is the second most common cancer in women worldwide and the first in under-developed and developing countries, which abide more than 80% of the global burden of the disease (WHO, 2010). Annually, it is estimated that 493,000 women worldwide will be diagnosed with cervical cancer and that 273,000 will die from the disease (Xiu-Zhen et al., 2012). South Asian countries like India, Nepal and Sri Lanka jointly contribute to nearly one-third of the global cervical cancer burden (Ferlay et al., 2010). There are a multitude of risk factors for cervical cancer worldwide (Raychaudhuri et al., 2012). There are therefore several risk factors for cervical cancer (viz HPV infection, sexual behaviors, p53 polymorphism and the characteristics of smoking) and these will in turn be related to tumorigenic potential (Sitakan et al., 2012). The age standardized rate (ASR) of cervix cancer for women in Nepal was found to be 17.6 for the year 2008 (Ferlay et al., 2010). Cervix cancer treatment is very expensive. Treatment options for cervical cancer depends on the stage of the tumor and includes surgery, radiotherapy, chemotherapy or their combination.

The precise forecasting of cancer trends and the estimation of future incidence rates allow better resource allocation, which is invaluable from public health standpoint. One approach to study incidence data on cancer is the analysis of trends and variations and creation of the best statistical prediction models. Sathian and colleagues made several attempts to forecast accurately the trend of communicable and non communicable diseases using statistical modelling in Nepal (Sathian et al., 2010a; 2010b; Sathian et al., 2010c; 2011a; 2011b). However, unlike many developed nations, Nepal lacks population based cancer registry (Sathian et al., 2010a;

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2010b; 2010c). Hence, statistical modelling for observing regional or national trends of cancer is challenging in the present scenario.

Manipal Teaching Hospital, being a tertiary care unit in the western region of Nepal, serves as a major catchment area for cervical cancer cases from the entire zone. In this hospital, 11.9% of cervical cancer cases received palliative care and rest, curative care during the time period between 2000 and 2008 (Sathian et al., 2010a). We studied these cases in order to estimate the numbers, and trends of cervix cancer cases visiting this hospital in 2015.

Materials and Methods

Forecasting of cervix cancer cases for radiotherapy was attempted using the data retrieved from the radiotherapy treatment records of patients treated at Manipal Teaching Hospital, Pokhara, Nepal, between September 2000 and December 2008. The variables collected were age, aim of treatment (curative vs. palliative), equipment used (Cobalt-60 or Linear accelerator) and information regarding unplanned interruptions and compliance to the treatment. Approval for the study was obtained from the institutional research ethical committee of the first author.

The data were analysed using Excel 2003, R 2.8.0 Statistical Package for the Social Sciences (SPSS) for Windows Version 16.0 (SPSS Inc; Chicago, IL, USA) and the EPI Info 3.5.1 Windows Version. The chi-square test was used to examine the association between different variables. A p-value of <0.05 (two tailed) was used to establish statistical significance. The annual numbers of patients visiting the centre for radiotherapy was then plotted against the corresponding year in the x axis. Curve fitting, also known as regression analysis, was used to find the "best fit" line or curve for a series of data points. Linear, Logarithmic, Inverse, Quadratic, Cubic, Compound, Power, Exponential and Growth models were chosen to fit to the obtained curve. The F-test was used for selecting the best fitting curve for the testing of hypothesis. P-value was taken as significant when <0.05 (two-tailed). R^2 values >0.80 were taken as significantly better for prediction (Beyer 1976; Chambers et al., 1983; Petrie et al., 2000; Sathian et al., 2010a; 2010b; 2010c; 2011a; 2011b).

Results

One hundred and fifty nine patients were found to have been treated with radiotherapy for cervix cancer during the study period. The patients' mean age was 54.42 years. Curative treatment was given to 88.1% (n=140) and palliative to the remaining 11.9% (n=19). Sixteen percent (n=25) did not complete the prescribed dose of radiation. 50.3 percent (n=80) of the cases were treated with Cobalt-60 and 49.7% (n=79) with Linear accelerator. Radiotherapy interruptions are known to adversely affect treatment outcomes. The study showed that unplanned treatment interruptions occurred in 34.6% (n=55) of the patients. The cubic model is a third degree polynomial, represented by the equation $y=m_0+m_1*x+m_2*x_2+m_3*x_3$, where m_0 is the constant term and m_1, m_2, m_3 are coefficient terms. Without the constant term, the equation of this model is $y=m_1*x+m_2*x_2+m_3*x_3$. This equation was the best fit equation in the forecasting of cancer cases from our data. Including the constant term none of the models

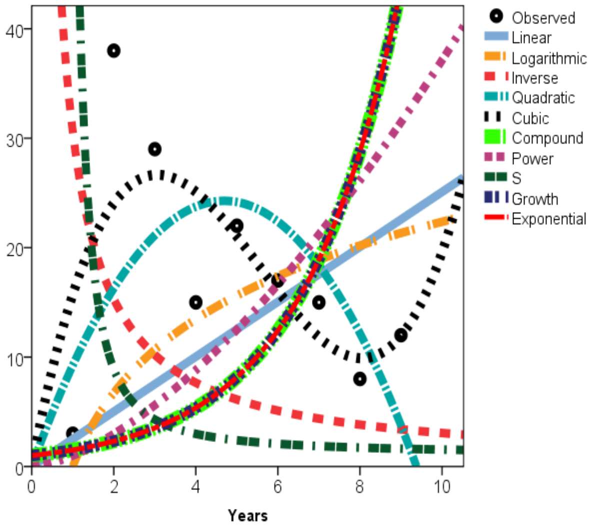

Figure 1. Fitted Curves for Observed Cervix Cancer Cases. (X-axis shows years; 1=2000, 2=2001, 3=2002, 4=2003 and so on, Y-axis shows number of cancer cases)

Table 1. Model Summary and Parameter Estimates Excluding the Constant Term for Different Models

Equation	R Square	P value	Parameter Estimates m1	m2	m3
Linear	0.482	0.026*	2.509		
Logarithmic	0.566	0.012*	9.712		
Inverse	0.387	0.055*	30.606		
Quadratic	0.791	0.004*	10.354	-1.104	
Cubic	0.871	0.004*	19.951	-4.500	0.27
Compound	0.734	0.002*	1.522		
Power	0.804	0.000*	1.570		
S	0.429	0.040*	4.371		
Growth	0.734	0.002*	0.420		
Exponential	0.734	0.002*	0.420		

*p<0.05 Statistically Significant

Table 2. Observed and Estimated Number of Total Cancer Cases from 2000-15

Year	Observed cases	Estimated cases	Lower Limit	Upper Limit
2000	3	16	-	40
2001	38	24	-	49
2002	29	27	-	52
2003	15	25	-	49
2004	22	21	-	45
2005	17	16	-	41
2006	15	12	-	37
2007	8	10	-	35
2008	12	12	-	41
2009	-	20	-	66
2010	-	34	-	114
2011	-	58	-	185
2012	-	92	-	284
2013	-	138	-	414
2014	-	198	-	577
2015	-	273	-	777

were best fitted. Excluding the constant term, cubic model was the best fitted (Figure 1, Table 1), with R^2=0.871 (p=0.004).

The equation for the cubic model for cervical cancer cases is $Y=19.951X-4.5X^2+0.270X^3$. In 2008, the observed and estimated numbers of cases were same. According to our model, 273 patients with cervical cancer are expected to visit the hospital in 2015 (Table 2).

Discussion

Our study has attempted to establish the applicability of statistical modelling in predicting the cervix cancer incidence in the regional context. Cervical cancer is the second most common cancer among women worldwide (Bradley, 2005). The South Asian countries like India, Bangladesh, Nepal and Sri Lanka jointly contribute to nearly one-third of the global cervical cancer burden (Ferlay et al., 2010). Study of the cervical cancer epidemiology in these regions is of utmost essence to cut down the regional as well as the global impact of cervical cancer.

Using the curve fitting method, we estimated the number and the trend of cervix cancer cases which had to receive radiotherapy at Manipal Teaching Hospital, Pokhara, from the years 2002-2015. The cubic model provided closely fitted curves for estimated and observed cancer cases (Figure 1). For each of the point estimate along the curve, confidence intervals have been calculated and are shown in Table 2.

In our study, the future annual estimated cervix cancer-cases (Table 2) showed an increasing trend of the disease. This is exactly opposite from the western world scenario where nearly 75% decrease in the incidence and mortality of cervical cancer has occurred over the past 50 years (Quinn et al., 1999; Willoughby et al., 2006). Multiple factors might have accounted for the increasing trend in cervical cancer incidence in this region. First of all, global incidence and mortality rates from cervical cancer are largely dependent on the strength of the screening programs and human papilloma virus (HPV) vaccination (Quinn et al., 1999; Willoughby et al., 2006). These interventions are weakly operational to virtually nonexistent in this region. This may also be reflection of lack of awareness of cervical cancer in this region. An awareness study by Teresa et al. in Nepal, India and Sri Lanka revealed less awareness of cervix cancer among the educated youth in these countries (Joy et al., 2011). Finally, the risk factor for cervical cancer may be highly prevalent and unaddressed in this region.

HPV is a necessary cause of cervical cancer, but it is not a sufficient cause. Other cofactors are necessary for progression from cervical HPV infection to cancer. Tobacco smoking, high parity, long-term hormonal contraceptive use, and co-infection with HIV have been identified as established cofactors. Co-infection with Chlamydia trachomatis and herpes simplex virus type-2, immunosuppression, and certain dietary deficiencies are other probable cofactors. Genetic and immunological host factors and viral factors other than type, such as variants of type, viral load and viral integration, are likely to be important but have not been clearly identified. Factors contributing to cervical carcinogenesis (cofactors) in Nepal are the prevalence of smoking, parity (fertility), oral contraceptive use, and HIV. The prevalence of smoking of any tobacco form in male and female was 29.9% and 22.6%, respectively (WHO, 2008). Cigarette smoking prevalence in male and female were 25.2% and 22.4%, respectively(WHO, 2008). Total fertility rate per woman was 3.3 (United Nations Secretariat, 2008). Oral contraceptive use was 3.5%.(United Nations, 2005). Adult (15-49 yrs) HIV prevalence percent were 0.5 with CI (0.4-0.7) (UNAIDS/WHO, 2008; WHO, 2008).

Sexual intercourse is the primary route of transmission of genital HPV infection. Information about sexual and reproductive health behaviour is essential to the design of effective preventive strategies against anogenital cancers. In Nepal, median age at first sexual intercourse among men (25-54 years) and women (25-49 years) were 19.6 years and 17.0 years, respectively. In males, extramarital sex in the last year was 5% and multiple partners in the last year among sexually active respondents aged 15-49 was 3% (Nepal demographic and health survey, 2006). These factors also constitute potential areas for intervention for cervical cancer reduction campaign in this area. Encouraging men to support women's participation in cervical cancer prevention program (Nene et al., 2007) may reduce the barrier. Therefore, it may be important to enhance awareness of cervical cancer among both husbands and wives for early detection of cervical cancer (Balaiah et al., 2012).

Our study has few limitations. First of all, the data is based on a hospital registry, and hence may suffer from selection bias to some extent. Further, patients treated with other aforementioned modalities were not included in the study. In the light of these limitations, the external validity of these data may be imperfect. Similarly, although the best fitting curve method has been a very popular method for forecasting in biostatistics, the limits of uncertainty are often wide and are reflected in the confidence limit of the point estimates as seen in our study. In the absence of a population based registry, a multi hospital centred study is often required to forecast the real situation of cervical cancer burden at a regional or national level.

Nonetheless, our study has initiated a positive crusade towards the epidemiological assessment of cervical cancer in the western region of Nepal. Given the huge and increasing burden of the disease, cervical cancer should be given high public health priority in this region and resource allocation should focus on eradication of factors that could have contributed to such increasing incidence of the disease.

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