A study on risk factors of cervical cancer among patients attending a tertiary care hospital: A case-control study

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ABSTRACT

Background: Cancer is an important health issue. According to the WHO report, globally, cervical cancer comprises 12% of all cancers in women and it is the leading gynaecological malignancy in the world. In many developing countries, it is the most common cancer among women where 85% of the estimated 493 000 new cases and 273 000 deaths in 2002 occurred worldwide.

Objectives: 1. To study the association between cervical cancer and parity. 2. To study the association between cervical cancer and other selected exposure variables

Settings and design: A hospital based case-control study was conducted in Shirdi Sai Baba Cancer Hospital and Research Centre, Manipal, Udupi District

Methods and material: A total of 273 participants (91 cases and 182 controls) were included. Information on demographics, habits, reproductive history, sexual history and menstrual history was taken using a semi-structured questionnaire. Statistical analysis used: Data was analysed using SPSS version 15. Univariate and Multivariate logistic regression was used to find out the association between the outcome and exposure variables. Results are expressed in odds ratio.

Results: Marital status (married) is an important risk factor for cervical cancer, OR = 2.98 (1.23–7.20). People having history of alcohol use were at 4.55 (1.17–17.73) times at risk of developing cervical cancer when compared to those who did not use alcohol. Age at menarche of 13–14 years was found to be a significant risk factor of cervical cancer with OR of 2.91 (1.18–7.20). Age at 1st coitus of <18 years had an odds ratio of 5.44 (2.73–6.38) and was significantly associated. At least one abortion is an important risk factor with odds of 2.61 (1.70–18.96). Also, adjusted odds ratio for parity of 3–5 was 3.16 (1.12–8.91) and 5.57 (1.70–18.96) for women having ≥6 parity when compared to women having parity of less than 3 and was statistically significant.

Conclusions: The study showed that marital status, history of alcohol use, <18 years of age at first coitus, age at menarche and parity of >3 as risk factors of cervical cancer

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1. Introduction

Cancer is an important health issue across the world. Globally, it accounted for 11.4 million new cases and 13% of all deaths (11.4 million) deaths in 2004.¹ Its incidence in SEAR in the year 2004 was 1.7 million.² Cancer has taken its place in top leading causes of death in India³ of which cervical cancer accounts for 17% of all cancer deaths⁴. However, distribution of cancer sites varies in

different parts of the world with the developing world carrying the major burden. An estimated 2 to 2.5 million cases of cancer are present in India at any given point of time⁵ and one quarter of global cervical cancer burden is borne by India alone⁴. The estimates show that cervical cancer may occur in every 1/53 women in developing countries as compared to 1/100 in developed region⁴. In Karnataka, about 1.5 lakh cases are present as prevalent cases and approximately 35,000 new cases are added to this each year.⁶ The consolidated report of cancer registries in South India reported stomach cancer for males and cervical cancer for females as the most common cancer sites.^{7–9} The age adjusted incidence of cervix cancer in urban India is 15–20 new cases per 100,000 women per year.¹⁰ According to WHO, in many developing countries, it is the most common cancer among women where 85% of the estimated 493 000 new cases and 273 000 deaths in 2002

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occurred worldwide.¹¹ In a study carried out in 1967, the risk factors of cervical cancer such as early marriage and delivery, number of partners and deliveries were identified as higher risk factors for cervical cancer.¹² Each cancer is unique and has various determinants; it differs from individual to individual and from one geographical location to the other. To my best knowledge, no risk-factor analysis has been carried out for cervical cancer in southern India- mainly in Udupi district. In past studies from across the world, personal hygiene, menstrual history and sexual history are shown to be associated with cervical cancer by some epidemiological studies done in different corners of world and India.^{12–28} The present study attempts to find out the various risk factors of cervical cancer among patients attending the tertiary care hospital – Shirdi Sai Baba Cancer Hospital, Manipal- in Udupi District.

2. Subjects and methods

2.1. Ethics statement

Ethical clearance was obtained from institutional ethics committee and hospital administration, Kasturba Medical College, Manipal University. The study participants were informed about the purpose, method and possible discomforts related with the questions and informed written consent was obtained.

2.2. Inclusion and exclusion criteria

All histopathologically confirmed cases of cervical cancer between the age group of 20–80 years were included in the study irrespective of their stages, and frequency matching for age ± 5 years was done (the available age range in the cervical cancer register was taken as the study participants age range); patient other than cervical cancer in the hospital were selected as controls. Cases, which were not willing to participate in study or those cases that were seriously ill were excluded from the study. Controls with first degree relatives, having personal history of cervical cancer and reproductive tract infection, pregnant women, women with gynaecological problems were excluded from the study. The cases and controls were interviewed using a semi-structured questionnaire.

2.3. Statistical methods

Sample size was calculated considering a parity of ≥ 3 (DLHS III) as a risk factor with an exposure of 20% in the control group and an

anticipated OR of 2 for a power of 80% and 5% level of significance. The calculated number of cases of cervical cancer was 91. For 1:2 allocation ratios the required number of controls were 182, hence 273 individuals were included in the study. Data analysis was done using statistical package for social sciences software. Data is summarized in form of tables. Univariate logistic regression analysis was used to evaluate the factors significantly associated with cervical cancer. Multiple Logistic Regression was used to calculate the adjusted Odds ratio with 95% CI.

3. Results and discussion

The study population included participants from urban and rural areas of 11 different districts of Karnataka. Udupi district had the maximum number of cases (52.7%). Maximum numbers of cases (41%) were in the age group of 51–60 years old followed by 34% in 41–50 year age group (Fig. 1). Age of the participants ranged from 35–78 years. Mean age of the study population was 53.2 years (± 9.8). In case group, the age of cases ranged from 35–77 year with mean age of cases is 54.2 (± 9.3). In control group the age of the participants ranged from 35–78 year. Mean age of the participants was 52.7 (± 10). Similar study was done by Biswas et.al¹⁵ which included participants from the age range of 25–70 years. Also, a study done by Shields TL et.al²⁴ included participants from the age range of 20–74 years. Table 1 shows the results of Univariate logistic regression for exposure variables education, marital status, habit of washing genitals, family history of cervical cancer, alcohol habit and diet. Habit of not washing genitals was found to be a risk factor of cervical cancer, but was not significant ($p = 0.073$). On the other hand, vaginal itching was a significant risk factor, which can be correlated with the findings of washing genitals. Similarly family history of cervical cancer was found to be significantly associated. When compared to vegetarians, people who consumed non-vegetarian diet were 2.260 (1.256–4.069) times more likely of getting cervical cancer. Education showed significant association with cervical cancer. People with primary education had an unadjusted odd ratio of 3.54 (1.59–7.87) which was highly significant with p -value 0.002. Also, illiteracy had unadjusted OR of 3.97 (1.85–8.54) with p -value of <0.001 . Similar findings were reported in a study done by Franceschi S et.al¹⁴ in Chennai which showed OR of 1.4 (0.7–2.8) for primary education and OR of 4.8 (2.7–8.4) for illiterate group when compared both with education level of high school and above. A study done by Taherian A et.al¹² in Iran showed OR of 4.6 (2.0–6.3, $p = 0.001$) for uneducated when compared to educated group.

Fig. 1. Age distribution of cases and controls.

Table 1

Univariate Logistic regression analysis for socio-demographic variables, habit and family history.

Variables	Category	Cases N = 91 Frequency (%)	Controls = 182 Frequency (%)	Crude OR (95% CI)	p-value
Education	High School and above	10 (11.0)	58 (31.9)	Reference	
	Primary education	33 (36.3)	54 (29.7)	3.544 (1.59–7.87)	0.002*
	Illiterate	48 (52.7)	70 (38.5)	3.977 (1.85–8.54)	<0.001**
Marital status	Married	76 (83.5)	141 (77.5)	1.473 (0.766–2.833)	0.10
	Widow	15 (16.5)	41 (22.5)	Reference	
Habit of washing genitals (after sexual intercourse)	Yes	23 (25.8)	67 (36.8)	Reference	
	No	66 (74.2)	115 (63.2)	1.672 (0.953–2.933)	0.073
Vaginal itching	Yes	30 (33)	23 (12.6)	3.515 (1.891–6.534)	<0.001**
	No	61 (67)	159 (87.4)	Reference	
Family history of cervical cancer	Yes	27 (29.7)	6 (3.3)	12.37 (4.884–31.356)	<0.001**
	No	64 (70.3)	176 (96.7)	Reference	
Alcohol	Yes	13 (14.3)	8 (4.4)	3.625 (1.44–9.00)	0.006*
	No	78 (85.7)	174 (95.6)	Reference	
Diet	Vegetarian	19 (20.9)	68 (37.4)	Reference	
	Non- Vegetarian	72 (79.1)	114 (62.6)	2.260 (1.256–4.069)	0.007*

* p < .05.

** p ≤ 0.01.

Table 2

Univariate Logistic regression analysis for menstrual factors.

Variables	Category	Cases Frequency (%)	Controls Frequency (%)	Crude OR (95% CI)	p-value
Age at menarche	<13 year	26 (28.6)	47 (25.8)	3.168 (1.424–7.050)	0.005*
	13–14 year	54 (59.3)	72 (39.6)	4.295 (2.067–8.924)	<0.001**
	>14 year	11 (12.1)	63 (34.6)	Reference	
Vaginal itching	Yes	30 (33)	23 (12.6)	3.515 (1.891–6.534)	<0.001**
	No	61 (67)	159 (87.4)	Reference	
Menopausal status	Pre-menopausal	9 (9.9)	52 (29.1)	Reference	
	Post- menopausal	82 (90.1)	130 (70.9)	3.743 (1.753–7.945)	0.001**
Age at menopause	Pre-menopausal	9 (9.9)	52 (29.1)	.368 (0.165–0.820)	0.014*
	<45	42 (46.2)	45 (24.7)	1.983 (1.128–3.483)	0.017*
	≥45	40 (44.0)	85 (46.7)	Reference	

* p < .05.

** p ≤ 0.01.

Table 2 shows the Univariate analysis for menstrual variables. Age at menarche and menopause were also significantly associated. Menopausal status was seen to be a risk factor for cervical cancer. A study done by Gyllensten U et al.²⁹ in Sweden to examine the value of screening for high-risk HPV in post-menopausal women showed that high-risk HPV were found in 6.2% (95% CI 5.2–7.3%) of the menopausal women. Another similar study done by

Singh B and Nalini N³⁰ in northern India-Jharkhand, found the incidence of cervical cancer in post-menopausal women to be 16%. When compared, these two studies in different setting although shows different sets of data, there is a wide difference in the incidence which may be due to the difference in genetic, racial and geographical profile.

Table 3

Univariate Logistic regression analysis for reproductive and sexual factors.

Variables	Category	Cases Frequency (%)	Controls Frequency (%)	Crude OR (95% CI)	p-value
Vaginal itching	Yes	30 (33)	23 (12.6)	3.51 (1.89–6.53)	<0.001**
	No	61 (67)	159 (87.4)		
Age at 1st pregnancy	<18	39 (42.4)	25 (14.6)	4.350 (2.402–7.877)	<0.001**
	≥18	52 (57.1)	145 (85.4)	Reference	
Abortion	None	61 (67)	163 (89.6)	Reference	
	At least one	30 (33)	19 (10.4)	4.219 (2.212–8.046)	<0.001**
Age at 1st coitus (in years)	<18	66 (72.5)	43 (23.6)	8.534 (4.810–15.142)	<0.001**
	≥18	25 (27.5)	139 (76.4)	Reference	
Parity	<3	8 (8.8)	70 (38.5)	Reference	
	3–5	40 (44.)	75 (41.2)	4.667 (2.043–10.66)	<0.001**
	≥6	43 (47.3)	37 (20.3)	10.169 (4.332–23.872)	<0.001**
Permanent methods	Yes	72 (79.1)	117 (64.3)	2.105 (1.168–3.796)	0.013*
	No	19 (20.9)	65 (35.7)	Reference	
Latency period (current age – age at 1st coitus)	<30	22 (24.2)	91 (50)	Reference	
	≥30	69 (75.8)	91 (50)	3.136 (1.424–7.050)	<0.001**
No of sexual partners	1	87 (95.5)	180 (98.9)	Reference	
	>1	4 (4.5)	2 (1.1)	4.286 (0.770–23.863)	0.097

* p < .05.

** p ≤ 0.01.

Table 4
Multivariate logistic regression.

Variables	Groups	Cases N (%)	Controls N (%)	Unadjusted OR (95% CI)	Adjusted OR(95% CI)	P value
Marital status	Married	76 (83.5)	141 (77.5)	1.473 (.76–2.83)	2.98 (1.23–7.20)	0.015
	Widow	15 (16.5)	41 (22.5)	1	1	
Habit of washing genitals (after sexual intercourse)	Yes	23 (25.8)	67 (36.8)	1	1	
	No	66 (74.2)	115 (63.2)	1.672 (0.95–2.93)	2.064 (0.98–4.34)	0.056
History of alcohol use	Yes	13 (14.3)	8 (4.4)	3.625 (1.44–9.00)	4.55 (1.17–17.73)	0.02
	No	78 (85.7)	174 (95.6)	1	1	
Age at menarche	<13 year	26 (28.6)	47 (25.8)	3.168 (1.42–7.05)	1.51 (0.55–4.13)	0.414
	13–14 year	54 (59.3)	72 (39.6)	4.295 (2.06–8.92)	2.91 (1.18–7.20)	0.020
	>14 year	11 (12.1)	63 (34.6)	1	1	
Age at menopause	Pre-menopausal	9 (9.9)	52 (29.1)	3.68 (0.165–0.820)	0.41 (0.14–1.14)	0.088
	<45	42 (46.2)	45 (24.7)	1.98 (1.12–3.48)	1.22 (.57–2.62)	0.594
	≥45	40 (44.0)	85 (46.7)	1	1	
Vaginal itching	Yes	30 (33)	23 (12.6)	3.51 (1.89–6.53)	4.00 (1.72–9.30)	<0.001
	No	61 (67)	159 (87.4)	1	1	
Age at 1st coitus (in years)	<18	66(72.5)	43(23.6)	8.53 (4.81–15.14)	5.44 (2.73–10.86)	<0.001
	≥18	25 (27.5)	139 (76.4)	1	1	
Abortion	None	61 (67)	163 (89.6)	1	1	
	At least one	30 (33)	19 (10.4)	4.21 (2.21–8.04)	2.61 (1.07–6.38)	0.035
Parity	<3	8 (8.8)	70 (38.5)	1	1	
	3–5	40 (44)	75 (41.2)	4.667 (2.043–10.66)	3.16 (1.12–8.91)	0.029
	≥6	43 (47.2)	37 (20.3)	10.169 (4.332–23.872)	5.57 (1.70–18.16)	0.004

p-value <0.05 = significant.

Bold values show statistically significant odds ratio.

Table 3 shows Univariate analysis for sexual and reproductive factors. Latency period which is calculated by subtracting current age with age at first coitus was seen to be significantly associated with cervical cancer. No. of sexual partners was not a significant risk factor in this study. Table 4 shows Multiple Logistic Regression analysis for risk factors of cervical cancer. Age at first coitus of <18 years showed high significance ($p < 0.001$) with cervical cancer with OR of 5.44 (2.73–10.86). Similar findings were observed in a study by Biswas N et al.¹⁵ which showed OR of 2.7 (0.8–8.9) with $p = 0.005$ for age at 1st coitus of <18 years. Parity was significantly associated with risk of cervical cancer. A study done by Franceschi et al.¹⁴ in Chennai showed similar findings for high parity (>4 vs. <2 births) OR=7.3 and for ≥3 vs. <3 births OR=3.01, but was insignificant. Biswas L. et al.¹⁵ also showed similar findings with OR=1.6 for parity of >3 ($p = 0.06$) and was significant. Age at menarche also had significant association with risk of cervical cancer. The adjusted odds ratio for age at menarche for <13 years was 1.51 (.55–4.13, $p = .414$) and or 13–14 years was 2.90 (1.18–7.20, $p = .020$) when compared to age at menarche of >14 years. In a study done by Reis N²⁰ in turkey, they showed a significant association between age at menarche and cervical cancer in chi square analysis. ($p = 0.001$).

4. Conclusion

Marital status (married), age at menarche of 13–14 years, history of vaginal itching, age at 1st coitus of <18 years, at least one abortion, parity of >3 are important risk factors of cervical cancer in this study. Health education can be given along with regular cervical cancer screening to women – especially post-menopausal women, and early and regular screening for women in reproductive age group; it will help in early diagnosis and prompt treatment. Introduction of HPV vaccination starting at early adolescent age group should be geared up in the public facilities as age at coitus <18 years is a risk factor. Focussed health programmes should be initiated to raise awareness to increase the informed health seeking behaviour in the high-risk group.

5. Limitations

The sample size was not enough to conclude many factors such as mode of delivery, OCP use, family history of cervical cancer etc.

Interviewer bias may be a limitation. Recall bias may be a problem. The study population is not a representative of general population, so the findings cannot be generalised.

Conflict of interest

None.

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