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Predictors of Cervical Cancer: A Matched Case-Control Study from Central India

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Abstract

Introduction:

Cervical cancer is the second most common malignancy among women in India and still continues to be a public health problem. The projected increase of cervical cancer cases is shown to be from 5,70,000 cases to 7,00,000 cases between 2018 and 2030. The purpose of this research had been to detect certain risk factors for cervical cancer, taking into account the prevalence of disease in India and the several factors that influence its occurrence.

Materials and methods

A hospital-based matched case-control study was conducted in a cancer institute among 243 cases of histopathologically diagnosed cervical cancer and 243 age group- and residence-matched controls. Risk factors were analyzed by calculating the odds ratio (OR) with a 95 percent confidence interval (95% CI). Multiple logistic regression was done for variables that were significant in bivariate analysis.

Results

Risk factors that were found to be significantly associated with the development of cervical cancer were low socioeconomic status, early menarche, age at coitus and first childbirth, higher parity, poor genital hygiene, and a history of tobacco chewing.

Conclusion

The study found several important associations between cervical cancer and several reproductive, socioeconomic, and hygiene factors. The results pointed out the need for socioeconomic upliftment, awareness of menstrual and genital hygiene, and education on reproductive health to reduce the burden of cervical cancer in India.

INTRODUCTION

Cervical cancer is the 4th most common cancer in women worldwide and most common genital tract malignancy [1]. It is the 2nd most common malignancy among women in India [2]. The disease is a prime example of global inequality in health, because, though the incidence of cervical cancer has now started to decline in developed countries, it is still a problem for public health. especially in developing countries where screening facilities are inadequate [3]. This issue is larger in low and middle income countries where nine out of ten deaths from cervical cancer have occurred [4].

Cervical cancer control was one of the priority interventions recommended for cancer control universally at World Health Assembly 2013, wherein a 2014–2020 NCD prevention and control action plan had been decided upon [5]. According to Hospital based cancer registries report in 2021, the relative proportion of cervical cancer was 15.2% of all cancers in women [6].

According to National cancer registry programme, there have been 342333 cases of cervical cancer prevalent in India in the year 2023, out of which, Maharashtra had 30414 cases [7]. As per Human papillomavirus and related cancers, fact sheet 2023, incidence rate of cervical cancer in India was 18.7 per 1,00,000 women [2]. The projected increase of cervical cancer cases is shown to be from 5,70,000 cases to 7,00,000 cases between 2018 and 2030 [4].

Numerous studies have demonstrated that high-risk human papillomavirus (HPV) is most important risk factor for development of cervical cancer [8]. Oncogenic subtype of HPV virus, particularly subtypes 16 and 18, is cause of cervical cancer among 12 high-risk HPV types [8, 9]. 95 percent of cervical cancers had been caused by persistent HPV infection of cervix if no treatment is received [10]. Early pregnancy, having several sexual partners, and coitus at a young age are some sexual health risk factors that can raise risk of cervical cancer. Cervical cancer has also been associated with smoking, poor hygiene, low socioeconomic level, several full-term pregnancies, and oral contraception. With right precautions, such as HPV vaccination, routine screening, avoiding risk factors, practicing good personal hygiene, etc., cervical cancer is avoidable.

Purpose of this research was to detect certain risk factors for cervical cancer, taking into account prevalence and incidence of disease in India and the several factors that influence its occurrence.

MATERIALS AND METHODS

Study design

This was a hospital-based matched case-control study conducted in a Cancer Institute in Central India from September 2022 to April 2024.

Study cases

The cases were histopathologically confirmed cervical cancer patients selected from Obstetrics and Gynaecology OPD, Radiotherapy OPD, Chemotherapy Ward and General Ward of a Cancer Institute in Central India, selected consecutively till sample size was achieved. Terminally ill patients, unable to share details, were excluded from the study.

Study controls

For controls, age group and place of residence matched patients attending outpatient departments of Urban and Rural health training centre affiliated to a tertiary health care institute in Central India were selected. Patients with current or past history of any cancer were excluded from the study.

Variables studied

The choice of risk factors to be studied were based on extensive literature search. The exposure variables studied were education, socioeconomic status, age at menarche, age at first coitus, age at first childbirth, parity, lifetime sexual partners, age of menopause, history of contraceptive use, genital hygiene, personal habits and family history of cancer.

Data collection

For sample size estimation, a study by Kadam D et al. was taken as reference [11]. The estimated sample size was 243 cases and 243 controls. Approval from the Institutional Ethics Committee (IEC) of Indira Gandhi Government Medical College, Nagpur had been obtained before commencing the study (IEC no: IGGMC.Pharm/BORS/1173-74/2022). Permission was taken from the Cancer Institute. A predesigned, pre-tested proforma was used as a tool for collection of the data by personal interview. All study participants have been explained about nature and purpose of study before starting the interview and information required. Written informed consent had been taken from every study participant in local language before starting the interview. Full cooperation of each study participant was confirmed. Confidentiality of the participants was assured and maintained throughout the study. A detailed interview regarding socio-demographic characteristics and risk factors for cervical cancer was taken. The clinical history of the participants was noted through their files.

Operational definitions

1. **Education & Occupation**: Classification as per revised Kuppuswamy socioeconomic status scale 2022 :[12,13]
2. **Socioeconomic status**: Classification was as per Modified B. G. Prasad [14, 15].
3. **Age at menarche**: The age at which the first menstrual period appeared in life [16].
4. **Age at first coitus**: The age of first sexual intercourse (in completed years).
5. **Age at first childbirth**: Age at which women gave birth to their first child.
6. **Age at menopause**: The age at which menstruation stopped completely resulting in permanent amenorrhea. Women who had no menstrual period in past 12 months were considered under “menopause attained” [16].
7. **Material used during menstruation**: Material (cloth or sanitary pad) used for major part of the reproductive life.
8. **Habit of tobacco chewing/smoking/alcohol**: Current and former users of the following were considered as “ever” having a habit and those who never consumed it were considered as “never”

having a habit [17].

Statistical Analysis

Data analysis had been performed by utilising statistical software Microsoft Office Excel 2020 and Jamovi 2.3.26. Quantitative data had been presented as mean and standard deviation, but qualitative data had been presented as numbers as well as percentages. Risk factors were analysed by calculating OR (odds ratio) with 95 percent confidence interval (OR; 95% CI). Multiple logistic regression was done for variables that were significant in bivariate analysis. P-value of less than 0.05 had been deemed statistically significant.

RESULTS

The study was conducted in a Cancer Institute in Central India. A total of 243 cases and 243 controls matched for age group and place of residence were enrolled for the study. This study was carried out with the purpose of studying some risk factors associated with cervical cancer.

Table 1
Distribution of study participants as per sociodemographic characteristics

Sociodemographic characteristics of study participants	Cases		Controls	
	No.	%	No.	%
Age				
35–44	39	16.05	39	16.05
45–54	101	41.56	101	41.56
55–64	77	31.69	77	31.69
65–74	26	10.70	26	10.70
Place of residence				
Urban	142	58.44	142	58.44
Rural	101	41.56	101	41.56
Education				
Professional degree	00	00.0	02	00.82
Graduate	07	02.88	27	11.11
Intermediate/ diploma	52	21.40	38	15.64
High school	61	25.10	81	33.33
Middle school	22	09.05	13	05.35
Primary school	37	15.23	30	12.35
Illiterate	64	26.34	52	21.40
Occupation				
Professional	00	00.00	02	00.82
Semi Professional	06	02.47	07	02.88
Clerical/shop/ farmer	12	04.94	15	06.17
Skilled worker	04	01.65	06	02.47
Semi skilled worker	15	06.17	22	09.05
Unskilled worker	65	26.75	51	21.00
Homemaker	138	56.79	133	54.73

Sociodemographic characteristics of study participants	Cases		Controls	
	No.	%	No.	%
Age				
Retired	03	01.23	07	02.88
Socioeconomic status				
Class I	02	00.82	08	03.29
Class II	50	20.58	74	30.45
Class III	79	32.51	97	39.92
Class IV	86	35.39	58	23.87
Class V	26	10.70	06	02.47
Marital status				
Married	201	82.72	215	88.48
Widow	39	16.05	28	11.52
Separated	02	00.82	00	00.00
Divorced	01	00.41	00	00.00

Table 1 shows sociodemographic characteristics of study participants. Participants have been matched for age group and place of residence. In both groups, maximum participants were in age group of 45–54years, that is 101 (41.56%). Mean age among cases was 54.1 ± 8.66 years, and in controls was 54.2 ± 8.93 years. It was seen that 142 (58.44%) cases and controls each resided in urban areas, 61(25.10%) cases and 81 (33.33%) controls had studied upto high school. Maximum cases 138 (56.79%) and controls 133 (54.73%) were homemakers. Most of the cases, 86 (35.39%) belonged to class IV socioeconomic class while most controls 97 (39.92%) belonged to class III. No participant reported having multiple sexual partners.

Table 2
Bivariate analysis of risk factors with cervical cancer

Risk factors	Cases (243)	Controls (243)	Odds ratio (95% CI)	p-value
	No. (%)	No. (%)		
Education				
Illiterate	64 (26.34)	52 (21.40)	1.31 (0.86–1.99)	0.201
Literate	179 (73.66)	191 (78.60)		
Socioeconomic status (SES)				
Low SES	112 (46.09)	64(26.34)	**2.39 (1.63–3.49)**	**< 0.001**
High SES	131(53.91)	179 (73.66)		
Age at menarche				
< 13 years	83 (34.20)	53 (21.81)	**1.85 (1.24–2.78)**	**0.002**
≥13 years	160 (65.80)	190 (78.19)		
Age at first coitus				
< 18 years	66 (27.16)	35 (14.40)	**2.21 (1.40–3.49)**	**< 0.001**
≥ 18 years	177 (72.84)	208 (85.60)		
Age at first childbirth				
< 18 years	35 (14.40)	19 (7.82)	**1.98 (1.10–3.57)**	**0.020**
≥18 years	208 (85.60)	224 (92.18)		
Parity				
> 3	58 (23.87)	32 (13.17)	**2.06 (1.28–3.22)**	**0.002**
≤ 3	185 (76.13)	211 (86.83)		
Age at menopause				
≤ 45 years	91 (45.73)	83 (40.29)	1.24 (0.84–1.85)	0.269
> 45 years	108 (54.27)	123 (59.71)		
Use of oral contraceptives				
Yes	37 (15.23)	33 (13.58)	1.14 (0.68–1.90)	0.605
No	206 (84.77)	210 (86.42)		
Use of condoms				
No	204 (83.95)	196 (80.66)	1.25 (0.78–2.00)	0.342

Risk factors	Cases (243)	Controls (243)	Odds ratio (95% CI)	p-value
	No. (%)	No. (%)		
Education				
Yes	39 (16.05)	47 (19.34)		
Washing genitals before coitus				
No	104 (42.80)	41 (16.87)	**3.68 (2.41–5.61)**	**< 0.001**
Yes	139 (57.20)	202 (83.13)		
Material used during menstruation				
Cloth	131 (53.91)	89 (36.63)	**2.02 (1.41–2.91)**	**< 0.001**
Sanitary pad	112 (46.09)	154 (63.37)		
History of tobacco chewing				
Ever	60 (24.69)	42 (17.28)	**1.57 (1.01–2.44)**	**0.045**
Never	183 (75.31)	201 (82.72)		
History of alcohol consumption				
Ever	08 (24.69)	07 (02.88)	1.15 (0.41–3.22)	0.793
Never	235 (96.71)	236 (97.12)		
Family history of cancer				
Yes	34 (13.99)	21 (08.64)	1.72 (0.96–3.06)	0.063
No	209 (86.01)	222 (91.36)		

Table 2 shows bivariate analysis of risk factors associated with cervical cancer. In terms of sociodemographic risk factors, it was found that women who were illiterate had higher risk of developing cervical cancer than women who were literate, this association was not statistically significant. Regarding socioeconomic status, classes I, II and III were clubbed together (high SES) and class IV and V (low SES) were clubbed together for analysis purposes. It was found that women who were from a low socioeconomic status, had higher risk of developing cervical cancer than women who were from a high socioeconomic status. (OR: 2.39; 1.63–3.49)

With regards to reproductive factors, it was observed that there was significant association of risk of cervical cancer with age at menarche < 13 years (OR = 1.85; 1.24–2.78), age at first coitus < 18 years (OR = 2.21; 1.40–3.49), age at first childbirth < 18 years (OR = 1.98; 1.10–3.57), parity > 3 (OR = 2.06; 1.28–3.22), not washing genitals after coitus (OR = 3.68; 2.41–5.61), using cloth during menstruation (OR = 2.02; 1.41–2.91). None of the study participants had taken the HPV vaccine.

Women who had a habit of tobacco chewing were found to have higher risk of developing cervical cancer. (OR: 1.57; 1.01–2.44). No significant association was found between habit of alcohol consumption and cervical cancer. In our study, there have been no smokers. A family history of cancer had been present in 34 (13.99%) of cases and 21 (8.64%) of controls. However, there had been no discernible link between cervical cancer and a family history of disease.

Table 3
Multiple logistic regression analysis for risk factors associated with cervical cancer

Risk factors associated with cervical cancer	Adjusted odds ratio (aOR)	95% C.I.		p-value
		Lower	Upper	
Low socioeconomic status	**1.96**	**1.26**	**3.04**	**0.003**
Age at menarche < 13 years	**2.02**	**1.31**	**3.11**	**0.001**
Age at first coitus < 18 years	1.19	0.57	2.51	0.630
Age at first childbirth < 18	0.76	0.31	1.84	0.552
Parity > 3	1.10	0.61	1.99	0.734
Not washing genitals after coitus	**3.28**	**2.06**	**5.21**	**0.001**
Using cloth during	1.17	0.73	1.86	0.499
Habit of tobacco chewing	0.92	0.55	1.54	0.753

Table 3 shows the multiple logistic regression analysis for the prediction of risk factors of cervical cancer. Multiple logistic regression analysis had been carried out considering occurrence of cervical cancer as the dependent variable and the various risk factors significant in bivariate analysis been used as independent variable for predicting the risk for each independent variable with the presence of other variables. After adjustments, it was found that who belonged to lower socioeconomic class, had menarche at less than 13 years of age and women who did not wash genitals after coitus were at 1.96, 2.02 and 3.28 times higher risk of developing cervical cancer respectively and this was found to be statistically significant. (aOR = 1.96, 2.02 and 3.28 respectively). Other traditionally recognized risk factors did not remain statistically significant in this multivariable model.

DISCUSSION

Cervical cancer is one of the most common cancers in women all over the world and still is a big public health challenge in developing countries especially India. Several epidemiological studies have shown the importance of identifying the risk factors associated with the development of cervical cancer for the planning of prevention strategies, increasing awareness and the promotion of early detection programs. The present matched case-control study tried to analyze the role of various demographic, reproductive,

hygienic, and lifestyle-related determinants among women with histopathologically confirmed cervical cancer and compare with healthy controls.

Age group matching was done and we found that the majority of study participants were between the ages of 45 and 54 years. Comparable results were reported in studies by Mohanan P et al. and Singini M et al., where the majority of research participants were between the ages of 45 and 54 years [18, 19]. This age bracket reflects the period when cervical cancer is most commonly diagnosed, often after years of persistent HPV infection. Our study discovered no significant relationship between risk of developing cervical cancer and education, in line with findings by Raghavendra B et al. [20]

We discovered that the risk of cervical cancer was 2.39 times higher among women with lower socioeconomic status. This shows that socioeconomic status plays a key role in cervical cancer. A study by Geetha B et al. had similar findings [21]. Lower socioeconomic status may influence risk through multiple pathways, including poor access to screening, limited awareness, suboptimal hygiene practices, early marriage, and higher parity.

Early menarche increases the risk of cervical cancer by causing early marriage and sexual engagement. It was found that age at menarche less than 13 years was associated with 1.85 times higher risk of developing cervical cancer. Our findings were similar to Sharma P et al. and Berraho M et al. [22, 23]. It was observed that women who had first coitus at less than 18 years of age were at 2.21 times higher risk of cervical cancer. Similar findings were observed by Sulistyawati D et al. [24]. This can be attributed to the fact that biological immaturity during adolescence makes the transformation zone of cervical epithelium more susceptible to HPV infection.

Our study found that women who had their first childbirth at less than 18 years of age were at 1.98 times higher risk of cervical cancer, in line with findings by Thakur A et al. [25]. Early childbirth may reflect early and prolonged exposure to sexual activity and HPV, as well as hormonal and cervical changes during pregnancy that may increase susceptibility. It was observed that women with a parity of more than 3 were at 2.06 times higher risk of cervical cancer compared to those with parity of 3 or less, which was similar to the study by Pratap P et al. [26]. Repeated cervical trauma, hormonal influences, and prolonged exposure to HPV may explain this association.

Our study also found that women who used cloth during menstruation were at 2.02 times higher risk of developing cervical cancer and this association was statistically significant, which was consistent with the study by Kashyap N et al. [27]. Reuse of inadequately cleaned cloth may lead to chronic genital infections and poor genital hygiene, which could facilitate persistent HPV infection.

In the present study, 60 (24.69%) cases and 42 (17.28%) controls had a habit of tobacco chewing. Habit of chewing tobacco was found to be significantly related with cervical cancer risk, similar to findings by Rajkumar T et al. [28]. The reason behind this could be that even though tobacco is not directly inhaled, its constituents and metabolites detected in cervical mucus can impair local immunity, thereby promoting persistence of HPV infection and carcinogenesis.

The study has several strengths and some limitations as well. In terms of strengths of the study, the study included almost every important risk factor in causation of cervical cancer with respect to all aspects – sociodemographic, reproductive, social factors. No similar study was conducted in this study area for the past decade, which helped us get an insight of the current scenario and associated factors compared to findings observed in previous studies. This was a matched case-control study to avoid confounding bias. However, since this study included prevalent cases and not only incident cases, there was possibility of recall bias. There is also likelihood of social desirability bias in disclosing personal habits or sexual partners. Despite matching and excluding controls with gynaecological complaints and history of cancers, we cannot eliminate the possibility of Berksonian bias.

CONCLUSION

The present hospital based matched case-control study was undertaken in a Cancer Institute in Central India to find out and assess the risk factors associated with cervical cancer. The study found several important associations between cervical cancer and several reproductive, socioeconomic and hygiene factors. Women of low socioeconomic status were more likely to develop cervical cancer (OR = 2.39). This association was statistically significant after multivariate analysis (aOR = 1.96). Early age at menarche below 13 years was also found to be an independent risk factor (aOR = 2.02). Poor genital hygiene practices especially not washing genitals after coitus had the strongest association with cervical cancer in both bivariate and multivariate (OR = 3.68; aOR = 3.28) analysis. Other factors also significantly associated on bivariate analysis were age at first coitus below 18 years, early age at first childbirth, multiparity, use of cloth during menstruation and tobacco chewing. The results underscored the importance of socioeconomic upliftment, awareness of menstrual and genital hygiene, and education on reproductive health to reduce the burden of cervical cancer in India.

Cervical cancer is a vaccine preventable cancer and as no participant took HPV vaccine, creating awareness regarding HPV vaccine is vital. People should be educated about risk factors of cervical cancer like tobacco chewing, early coitus, early first birthing age, increased parity, poor genital cleanliness.

Declarations

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Consent to participate: Yes

Consent to publish: Yes

Clinical trial number: Not applicable

Data availability statement: The datasets generated during and/or analysed during the current study are not publicly available but are available from the corresponding author on reasonable request.

Conflict of interest: There is no conflict of interest.

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