Research Article

CONTRIBUTING FACTORS IN PREDISPOSITION OF SYMPTOMS OF CERVICAL CANCERS IN UNSCREENED POPULATION OF NORTHERN INDIA

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ABSTRACT

Problem considered: The huge disease burden and the potential for prevention through screening makes cervical cancer control program an important area of action in developing countries. The present study explores the risk factors related to symptoms of cervical cancer.

Materials and methods: 2038 females were surveyed by trained personnel and analyzed for symptoms and risk factors for cervical cancer.

Results: The primary symptoms were painful micturition in 8.0% followed by white discharge (7.1%), and pelvic pain (3.1%). Painful micturition were significantly associated with age 35–44 years (p<0.01). Whitish discharge was statistically related to the different age groups as <25 years, 25-34 years, 35-44 years (p<0.001/=0.03/<0.001). The abnormal age of menarche (≤11 or ≥16 years) (p<0.05) and >3 times of pregnancy were also significantly associated with white discharge (p<0.05). Pelvic pain was significantly related to <25 years, 25-34 years (p<0.05/<0.05). It was also related to the abnormal age of menarche (p=0.02) and highly associated with >3 times of pregnancy (p<0.05).

Conclusion: The early identification of risk factors for cervical cancer is important in terms of early detection and prevention. Efforts should be made to innovate ways to reach and educate women.

INTRODUCTION

There is a marked difference in the distribution of cancer sites across different regions of the world. Cancer of uterine cervix is one of the leading causes of cancer deaths among women worldwide. In contrast to developed countries, cervical cancer is a major public health problem in developing countries like India, and India alone accounts for one‑quarter of the worldwide burden of cervical cancers[1,2]. It is the one of the leading cause of cancer mortality, accounting for 17% of all cancer deaths among women aged between 30 and 69 years. It is estimated that cervical cancer will occur in approximately 1 in 53 Indian women during their lifetime compared with 1 in 100 women in more developed regions of the world[2]. In India, cervical cancer contributes to approximately 6–29% of all cancers in women.

The age‑adjusted incidence rate of cervical cancer varies widely among registries; highest is 23.07/100,000 in Mizoram state and the lowest is 4.91/100,000 in Dibrugarh district[3]. Every year in India, 122,844 women are diagnosed with cervical cancer and 67,477 die from the disease. India has a population of 432.2 million women aged 15 years and older who are at risk of developing cancer. It is the second most common cancer in women aged 15–44 years. India also has the highest age standardized incidence of cervical cancer in South Asia at 22, compared to 19.2 in Bangladesh, 13 in Sri Lanka, and 2.8 in Iran[4].

The epidemiology of cancer cervix has been very challenging. Various studies have confirmed the link with sexual activity, multiparity, early marriage, multiple sexual partners, illiteracy, and low socioeconomic status. Human papillomavirus (HPV) infection, particularly with type 16, 18, is quite likely the cause of cervical carcinogenesis. Most of the women infected with HPV do not develop invasive cervical carcinoma. It is only in a proportion of women in whom the infection is persistent and several other cofactors that persist help in the development of disease[5].Unlike other cancer sites, cervix can be subjected to screening for early diagnosis and treatment. However, despite availability of various cervical cancer screening methods, as

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well as large burden of disease in India, there is no countrywide government‑sponsored public health policy on prevention of cervical cancer by either screening or vaccination or both. Socio-demographic and reproductive factors are major cofactors for the development of cervical cancer, and cervical cancer mainly affects the socioeconomically disadvantaged women[6]. The huge disease burden in developing countries and the potential for effective prevention through screening makes of cervical cancer control an important area of action for any cancer control program in developing countries[7].

Therefore, this study was carried out to understand the risk factors and symptoms related to the gynaecological cancer among females of unscreened population of western parts of Uttar Pradesh and eastern Rajasthan. The main reason behind selecting these areas was the higher number of reported patients with cervical cancer from the region.

MATERIAL AND METHODS

Study subjects

The fundamental purpose of screening camps was to spread awareness regarding the various risk factors and symptoms associated with gynaecological cancer among females of unscreened population of northern parts of India. One-to-one interaction was done at the certain places to make sure the maximum availability of females to approach camps on the specified dates before the screening camps.The participants were the individual females who came to screening camp voluntarily on day of survey. Females of age group (14 -85 years) were included in the survey. Females with any serious disease and those who had not given consent were excluded from the screening program. A pilot study was also conducted to pre-test the questionnaire before carrying out the screening camps. The findings of the pilot study provided useful information helped in improving the clarity of questions for finalization of the questionnaire. The internal consistency of the questionnaire was estimated to be 78% using Cronbach's alpha which indicated a good level of reliability.

Data collection

Present study is a part of ongoing community-based outreach health camp organized by Nayati Charitable trust, a part of Nayati Medicity, Mathura, India. A total of 55 screening camps were organized between April 2015 and May 2017 in unscreened population of western Uttar Pradesh and Eastern Rajasthan. A pretested, self-administrable and designed questionnaire was used to collect the information regarding various risk factors and symptoms of cervical cancer. The study subjects were interviewed by skilled health workers who were sensitized and trained in basic cancer screening under observation of qualified medical graduates and randomly cross checked by medical doctors. A total of 2038 females of age groups (14 to 85 years) were analyzed for associated risk factors and symptoms for cervical cancer. The study variables included age, marital status, age at marriage, age at menarche, and age at menopause, age at first childbirth, abortion, painful micturition, vaginal discharge and regarding pelvic pain.

Statistical analysis

All scale variables were presented as mean ±SD and categorical with respective proportions. Data of various risk factors namely current age, age at marriage, age at first childbirth, age at menarche and age at menopause, etc. were analyzed to calculate the magnitude of association with the prevalence of common symptoms of painful micturition, white discharge and pelvic pain. Statistical tests such as chi-square and Student's't' were applied to examine the association and differences wherever applicable. Multivariable logistic regression analysis was applied to estimate the adjusted odds ratios (AOR) with respect to reference category for comparison and magnitude of the association. Data were entered and coded in MS Excel (version 2007) and analyzed using IBM SPSS 21.0 (Armonk, NY, USA).

RESULTS

Characteristics of the study population

In this study 2038 females of all age groups ranging from 14-85 years were screened for symptoms related to gynaecological cancer at different health camps in various parts of Northern India.

Table 1 shows background demographic and prevalence of symptoms. The mean age of the females was (42.3 ± 14.5 years), and more than 90% were married. The mean age at menarche was nearly fourteen years (13.8 ± 1.6 years), age at marriage was nineteen years (18.8 ± 2.7 years), age at first childbirth was twenty-one years (21.2 ± 2.2 years), and age at menopause was forty-five years (45.1 ± 2.9 years). The number of pregnancies in 1912 eligible females were none(14.4%), one time(38.3%), two times(21.4%), three times(14.3%), four or more times (11.5%), having number of living children's none(16.3%), one(38.1%), two(25.3%), three or more(20.3%) and 92.2% had no history of abortions at the time of screening. The prevalence of painful micturition was found to be 8.0% followed by white discharge per vagina 7.1% and pelvic pain 3.1%.

Table 1 Background profile of females screened for cervical cancer

Background variables	(mean±SD)	
Total female screened	2038(100)	
Current age of females (years)	42.3±14.5	
Age at marriage (years)	18.8±2.7	
Age at menarche (years)	13.8±1.6	
Age at menopause (years)	45.1±2.9	
Age at first child birth (years)	21.2±2.2	
Marital status(n=2038)	Number	%
Unmarried	126	6.2
Married	1888	92.6
Widow	24	1.2
Number of pregnancies among married and widow women(n=1912)		
Non pregnant	276	14.4
One time	733	38.3
Two times	410	21.4
Three times	273	14.3
Four or more times	220	11.5
Number of women having living children (n =1912)		
no child	312	16.3
one child	728	38.1
two children	483	25.3
three or more children	389	20.3
Number of women underwent abortions (n =1912)		

no abortion	1762	92.2
One or more abortion	150	7.8
Symptoms for gynecological cancer		
Painful micturition	163	8
White discharge per vagina	144	7.1
Pelvic pain	63	3.1

Association between factors and symptoms

Table 2 shows observed association between factors variables with three symptoms, i.e. painful micturition, white discharge and pelvic pain. The prevalence of painful micturition was maximum in age group 35-44 (31.9%), white discharge per vagina and pelvic pain was highest in the age groups 25–34 years was found to be 34.7%, and 34.9% respectively and the

vagina and pelvic pain respectively among the females who married in 18–20 years of their age but was not statistically significant. The majority of females (94.35%) started their menstruation cycle at 12–15 years of age. The painful micturition, white discharge and pelvic pain were statistically related ($p < 0.05$) with the proportionate variation in distribution of females according to age of menarche. Prevalence of pelvic pain (55.7%) was found to be higher among the females having time interval between marriage and menarche less than five years ($p < 0.05$). The proportion of symptoms was found to be maximum among the females who experienced one or two pregnancies, and it was statistically significant with painful micturition ($p < 0.001$), white discharge per vagina ($p < 0.005$) and pelvic pain($p <0.005$).

Table 2 Association of different symptoms with risk factors of Cervical cancer

Risk factor variables	Total	Symptoms for gynecological cancer					
		Painful micturition n(%)	P value	White discharge per vagina n(%)	P value	Pelvic pain n(%)	P value
Age group (years) (n=2038)							
<25	224	17 (10.4)		27 (18.8)		9(14.3)	
25-34	385	34 (20.9)		50 (34.7)		22(34.9)	
35-44	495	52 (31.9)	0.009	43 (29.9)	<0.001	20(31.7)	<0.001
45-54	437	38 (23.3)		15 (10.4)		9(14.3)	
>=55	497	22 (13.5)		9 (6.3)		3 (4.8)	
Marital status (n=2038)							
Unmarried	126	12 (7.4)		7 (4.9)		2(3.2)	
Married	1888	151 (92.6)	0.289	137 (95.1)	0.306	61(96.8)	0.399
Widow	24	0		0		0	
Age at marriage (years) (n=1912)							
<18	450	45 (29.8)		35 (25.5)		19 (31.2)	
18-20	1154	79 (52.3)	0.181	82 (59.9)	0.668	39(63.9)	0.078
21-24	245	21 (13.9)		14 (10.2)		3 (4.9)	
>=25	63	6 (4.0)		6 (4.4)		0	
Age at menarche (years) (n=2038)							
<=11	33	1(0.6)		7 (4.9)		4 (6.3)	
12-13	633	31 (19.0)	<0.001	51 (35.4)	0.006	16(25.4)	0.014
14-15	1290	130 (79.8)		81 (56.3)		39(61.9)	
>=16	82	1 (0.6)		5 (3.5)		4 (6.3)	
Duration between age at marriage and menarche (years) (n=1912)							
<5	853	75 (49.7)		60 (43.8)		34(55.7)	
5-9	929	66 (43.7)	0.417	67 (48.9)	0.961	27(44.3)	0.043
>=10	130	10 (6.6)		10 (7.3)		0	
Age at menopause (years) (n=943)							
<45	464	33 (51.6)	0.696	16 (61.5)	0.202	8 (61.5)	0.370
>=45	479	31 (48.4)		10 (38.5)		5 (38.5)	
Age at first child birth (years) (n=1846)							
16-18	143	28(18.8)		18(13.7)		8(13.3)	
19-21	846	63(42.3)	<0.001	65(49.6)	0.019	33(55.0)	0.028
22-24	719	46(30.9)		41(31.3)		19(31.7)	
>=25	138	12(8.1)		7(5.3)		0	
Number of pregnancies among married and widow women (n=1912)							
Non pregnant	276	7(4.6)		13 (9.5)		2 (3.3)	
One time	733	91 (60.3)	<0.001	72 (52.6)	0.004	29(47.5)	0.004
Two times	410	23 (15.2)		22 (16.1)		7 (11.5)	
Three or more times	493	30 (19.9)		30 (21.9)		23(37.7)	
Number of women having living child (n=1912)							
No child	312	12 (7.9)	<0.001	15(10.9)	0.003	2(3.3)	
One child	728	86 (57.0)		70 (51.1)		29(47.5)	<0.001
Two child	483	24 (15.9)		22 (16.1)		7(11.5)	
Three or more child	389	29 (19.2)		30(21.9)		23(37.7)	
Number of women underwent abortions (n=1912)							
No abortion	1762	149 (98.6)	<0.001	136(99.3))	<0.001	60(98.4)	0.085
One or more abortions	150	2(1.4)		1 (0.7)		1 (1.6)	

distribution of symptoms was statistically associated ($p < 0.05$) with age. Married women had higher number (>90%) of cases with the symptoms as compared to unmarried/widow females. Prevalence of symptoms was reported to be higher 52.3%, 59.9% and 63.9% for painful micturition, white discharge per

Similarly females with one or two living children were also showing a higher occurrence of symptoms: painful micturition ($p < 0.001$), white discharge per vagina ($p< 0.005$) and pelvic pain($p<0.001$). Out of 1912 eligible women, majority (92.2%) had not undergone any abortion. Also, their distribution was

showing association with painful micturition and white discharge (p<0.001).

Independent risk factors

Multivariable logistic regression was used to explore the independent risk factors for the occurrence of symptoms related to cervical cancer (Table 3).

treatment of cervical cancer, precursor lesions and cervical cancer are still continues to be a public health problem in India. The age-adjusted incidence rates of cancer cervix reported by majority of Indian cancer registries are much higher than the world age-adjusted incidence rate

Table 3 Multivariable logistic regression analysis for factors associated with gynecological cancer related symptoms

Predictors of symptoms	Painful micturition		White discharge		Pelvic Pain	
	AOR	95% C.I.	AOR	95% C.I.	AOR	95% C.I.
Age group (years)						
<25	1.6	0.7-3.5	11.5**	5.0-26.6	12.2*	3.0-49.7
25-34	1.7	0.9-3.1	7.9**	3.8-16.7	12.3*	3.6-42.4
35-44	2.0*	1.2-3.5	5.1**	2.4-10.8	6.6*	1.9-23.1
45-54	1.9*	1.1-3.4	1.8	0.7-4.2	3.4	0.9-12.8
>=55 ®						
Marital status						
Unmarried/Widow ®						
Married	0.3	0.1-1.2	1.2	0.2-6.2	-	-
Age at marriage (years)						
<18	0.7	0.4-1.1	1.1	0.6-2.0	1.06	0.5-2.1
18-20	0.9	0.4-2.2	0.8	0.3-2.2	0.3	0.0-1.6
>=21®						
Age at menarche (years)						
Normal age (12-15) ®						
Beyond normal (<=11 or >=16)	0.1*	0-0.8	2.0*	1.0-3.9	2.5*	1.1-5.8
Duration between age at marriage and menarche (years)						
<5	1.2	0.4-3.3	0.8	0.3-2.3	-	-
5-9	1.1	0.4-2.7	1.1	0.4-2.9	-	-
>=10 ®						
Age at 1st child birth (years)						
16-19	1.5	0.7-3.5	1.4	0.6-3.3	0.6	0.2-2.3
20-23	1.2	0.6-2.4	0.7	0.3-1.4	0.6	0.2-1.8
>=24 ®						
Number of pregnancies among married and widow women						
Not pregnant ®						
One time	4.4**	1.9-10.0	2.3	1.1-4.8	5.1*	1.1-22.6
Two times	1.8	0.7-4.3	1.2*	0.5-2.8	2.1	0.4-10.8
Three or more times	2.5*	1.0-6.0	1.9*	0.8-4.4	8.1*	1.7-37.5

AOR: adjusted odds ratio; C.I.: confidence interval; ®: reference category
*-P value <0.05,**- P value <0.001

It shows that chances of developing painful micturition were significantly associated with age 35–44 years (AOR =2.0, 95% CI: 1.2–3.5, p < 0.01). It was also observed that risk was highest for those who were at least one time pregnant (AOR = 4.4, 95% CI:1.9-10.0, p <0.001). Risk of occurrence of white discharge per vagina was statistically related to the different age groups as < 25 years (AOR = 11.5, 95% CI: 5.0–26.6, p < 0.001), 25–34 years (AOR = 7.9, 95% CI: 3.8–16.7, p < 0.001) and 35–44 years (AOR = 5.1, 95% CI: 2.4–10.8, p < 0.001) with reference to age ≥ 55 years. It was also associated with the abnormal age of menarche (AOR = 2.0, 95% CI: 1.0–3.9, p < 0.05) as compared with the normal age of start (12–15 years). Three or more times of pregnancy was also significantly associated with white discharge (AOR = 1.9, 95% CI: 0.8-4.4, p < 0.05). The likelihood of developing pelvic pain was significantly related to the females < 25 years (AOR = 12.2, 95% CI: 3.0–49.7, p < 0.05) and 25–34 years (AOR = 12.3, 95% CI: 3.6–42.4, p < 0.05) as compared to >55 years of age. Risk of pelvic pain was also related to the abnormal age of menarche (≤11 or ≥16 years) (AOR = 2.5, 95% CI: 1.1–5.8, p = 0.02) and with three or more times of pregnancy (AOR=8.1, 95% CI:1.7-37.5, p<0.05).

DISCUSSION

In today's era, in spite of the availability of HPV vaccines, affordable and effective methods for early detection and

of 7.9/100,000 population but is lower or similar to cervical cancer incidence rates of 19.2/100,000 population seenin the South-East Asian region[1]. The high burden of cervical cancer in India and South-East Asian countries is due to poor to moderate living standards, early marriage, multiparity, a high prevalence of HPV, and due to lack of screening[8].

In this study 2038 females of all age groups ranging from 14-85 years were screened for symptoms related to gynaecological cancer at different health camps in various parts of Uttar Pradesh and Rajasthan. The common symptoms related to cervical cancer reported in this study were painful micturition (8.0%), white discharge per vagina (7.1%) and pelvic pain (3.1%). The prevalence of these symptoms are comparable with our previous results[9]. A hospital based study by Gupta *et al* reported that the prevalence of 8.1% for painful micturition, 36.3% for white discharge per vagina and 54.9% for pain in the lower abdomen. The reported prevalence of burning micturition was similar but white discharge per vagina and lower abdominal pain was lower in our results as compared to Gupta *et al* from the same region[10]. Satyanarayana *et.al.* reported the common presenting symptom was abnormal vaginal discharge in 60% women followed by 36.5% lower abdominal pain and 22% backache, only few women (0.6%) presented with post coital bleeding in selected rural community of north india[11]. In our study age of menarche

was 12-15 years in most of the cases (94.3%) and lower abdominal pain (55.7%) was higher among females having time interval between marriage and age of menarche <5 years. Ruiz *et al* reported greater risk of cytologic abnormalities in women those with first sexual intercourse (FSI) within 3 years of menarche when compared with women who postponed FSI beyond 3 years of menarche[12]. A study by Natphopsuk *et al* showed that the interval between age at menarche and first sexual intercourse <6 years resulted in a significant increase in the risk for cervical cancer[13]. Similar finding seen in study by Akman *et al*[14]. In present study the prevalence of these symptoms was found higher in married women (90% cases) as compared to unmarried women and prevalence of symptoms was higher 52.3%, 59.9% & 63.9% for painful micturition, per vaginal whitish discharge and lower abdominal pain who married in 18-20 years of age. Sierra-Torres CH *et al* reported the risk factor of developing gynaecological malignancies is two folds higher in women who marry before 16 years of age compared to those marry after 20 years of age[15]. In a study, women marrying before the age of 18 years were found to be almost 3 times at risk (AOR = 2.88) as compared to women marrying after the age of 18 years[16]. In this study these symptoms was maximum among females who have 1 or more pregnancies statistically significant with painful micturition (p < 0.001), whitish discharge (p < 0.005), and pelvic pain (p < 0.005). In a study high parity with >3 children was found to be a significant risk factor (AOR: 2.88) was showing similar results[16]. Bayo S *et al* did a pooled analysis of 10 case-control studies on HPV-positive women, found the risk becoming twice higher with the number of pregnancies[17]. The study found that women of increasing age and with a large number of pregnancies to be at a significantly higher cervical cancer risk in the rural population in India. Cervical cancer is rarely reported among women under the age of 30 years but the prevalence of HPV infection is at its peak under 30 years old[18]. Parity is probably a good marker of hormonal environment throughout the fertile years of women, as well as a marker of repeated cervical trauma predisposing to infection.

In present study risk of occurrence of discharge per vagina was statistically related to the different age groups as < 25 years (p < 0.001), 25–34 years (p = 0.03) and 35–44 years (p < 0.001) with reference to age ≥ 55 years. A national descriptive study in U.K done for early age group less than 30 years, patient sign and symptoms were more common in patients < 25 than patients aged 25–29 (40% versus 15%, p = 0.16)[19].

CONCLUSION

Risk factors such as age at birth of first child, age at marriage, multiparity and sign, symptoms like pelvic pain, per vaginal whitish discharge, painful micturition were highly prevalent among the cases and the association was found to be significant statistically. Efforts should be made to innovate ways to reach, educate women in rural and semi-urban northern India. The identification of risk factors for cervical cancer is important in terms of early detection, primary and secondary prevention.

Limitations

In the present study, data were analyzed of the females who approached to screening camps. It may be possible that women with high socioeconomic status are less likely to attend the screening camp than with low socioeconomic status. Non-

availability of histopathological findings of the suspected cases may also have restricted the estimation of cancer prevalence. A small fraction of women reporting problems is also a limitation in this study. Data related to the important risk factors such as socioeconomic condition, diet habits, and long term use of oral contraceptives and intra uterine device were not obtained. In the subsequent rounds, the added important factors and pathological facilities may improve the confirmatory findings of cancer with additional clinical outcomes.

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