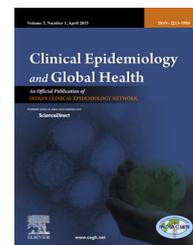


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Original Article

Level and determinants of precancerous symptoms of cervical cancer in unscreened population of Uttar Pradesh and Rajasthan, India: A pilot study

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ABSTRACT

Problem considered: Cervical cancer, mainly caused by human papillomavirus infection, is one of the most frequent cancers in women in the developing world including India. The present study attempts to explore the risk factors related to symptoms of cervical cancer. **Materials and methods:** A total of 1319 females of age groups ranging from 14 years to 85 years were included in the present study and analyzed for symptoms and risk factors for cervical cancer.

Results: The prevalence of painful micturition, white discharge per vagina, and pelvic pain in the age group 25–44 years was found to be 22.1%, 21%, and 8%, respectively, and the distribution of symptoms was statistically associated ($p < 0.05$) with age. Chances of developing painful micturition were significantly related to age group 45–54 years (AOR = 2.5; 95% C.I.: 1.4–4.5), while the likelihood of developing pelvic pain was significantly related to the females of age groups of below 25 years (AOR = 8.4; 95% C.I.: 1.4–12.1) and 25–34 years (AOR = 7.9; 95% C.I.: 1.7–8.3). Pelvic pain was also independently related to the abnormal age of menarche (≤ 11 or ≥ 16 years) (AOR = 3.6; 95% C.I.: 1.6–8.5) concerning the standard age of start.

Conclusions: Findings of the study indicate that there is lack of awareness about the key risk factors for cervical cancer among women that pointed out the issue of limited knowledge which may work as an obstacle in health services utilization.

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1. Introduction

With 0.49 million new cases, cervical cancer is seventh leading cancer overall and ranked fourth in women throughout the

globe and is responsible for more than 0.24 million deaths per year in 2013.¹ Approximately 90% of cases, as well as deaths from cervical cancer, occurred in developing countries.² It is ranked as the third most common cancer overall, and the second most common cancer in the female population in India

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causing approximately 0.12 million new cases and 68,000 deaths per year.¹

The cervical cancer is much more prevalent among women of low socio-economic status as well as among rural women in India.³ The estimated age-standardized cervical cancer incidence and mortality rates were reported to be 30.7 and 17.8 per 100,000 women respectively, and peak incidence was observed among older women.⁴ Ganjewala,⁵ indicated that the cervical cancer alone represents 34% out of all carcinoma prevalence in some parts of Uttar Pradesh and Madhya Pradesh. The national cancer registry program (NCRP) reported highest incidence of cervical cancer in Uttar Pradesh in 2009 with a total of 17,367 cases that increased to 18,692 in 2012.⁶ Numerous epidemiological studies in present and past have significantly contributed to understanding about cancer-associated symptoms and risk factors.⁵

It is a well-known fact that persistent infection with human papilloma virus (HPV) of specific high-risk types is the significant cause of development of almost all types of cervical cancers and their precancerous lesions.⁷ The infection also being precipitated by other exogenous or endogenous cofactors, which includes but not limited to sexual habits, reproductive history, other sexually transmitted diseases, smoking, nutritional deficiencies and genetic susceptibility, acting in conjunction with HPV may be necessary for the disease progression.^{8,9}

It has been established that different socio-demographic and reproductive factors can influence the participation in screening programs related to cervix cancer. Some of them are the age of individual, education, marital status, income, a number of children alive, present use of contraception, region, lack of awareness about cervical cancer screening and its prevention, personal and lifestyle factors, etc.¹⁰

A hospital based study showed that the risk factors which lead to developing cervical cancer includes multiparity, long-term use of oral contraceptives, use of copper-T for continuously more than 5 years, sexually transmitted diseases, HIV infection, smoking/tobacco chewing, genital warts, poor hygienic conditions, reproductive tract infections and low intake of fruits and vegetables due to low socio-economic status.¹¹ The common symptoms included hemorrhage, leucorrhoea, cachexia and pain (knee, leg and back) and other symptoms might be painful and frequent micturition, incontinence of urine, painful defecation and pruritus because of vaginal discharge.⁶ There was no conclusive evidence that suggests association of use of oral contraceptives with cervical cancer.¹² According to some reports, the age of women is not a prognostic factor in carcinoma of the cervix.¹³ Other authors have noted decreased survival in women younger than 35 or 40 years, who have a greater frequency of poorly differentiated tumors.¹⁴ It was also reported that early age at first intercourse, history of multiple sexual partners, and a higher number of pregnancies are risk factors.⁶

Cervical cancer prevention programs have failed to meet their objectives due to logistical, financial, and social problems.¹⁵ Major barriers to screening uptake include lack of awareness about the disease, lack of attitude toward the concept of prevention, the geographical and economic inaccessibility to health care, the poor quality of health care

delivery services and a lack of support from family members including husband.¹⁶

2. Materials and methods

2.1. Study samples

The purpose of screening camps was to spread awareness regarding the risk factors and symptoms related to the gynecological 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.⁵ Before the screening camps, a small one-to-one interaction was done at the selected places to make sure the maximum availability of females to approach camps on the specified dates. The participants were the individual females of all age group who came to screening camp voluntarily on day of survey. No specific criterion was set for the selection of females to the screening. However, the females with any serious illness and those who had not given consent were excluded from the screening program. A pilot study was also conducted to pretest the questionnaire in selected study areas of western Uttar Pradesh prior to carrying out the screening camps. The results of the pre-testing provided useful information helpful 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 that indicated a good level of reliability.

2.2. Data collection

A total of 26 screening camps were organized at different places in western Uttar Pradesh and eastern Rajasthan during period of April 2015 to June 2015. A pretested, designed, and self-administrable questionnaire was used to collect the information from participants regarding risk factors and symptoms of cervical cancer. The study participants were interviewed by trained health workers who were sensitized and trained in basic cancer screening under supervision of qualified medical graduates and randomly cross checked by medical doctors. Data of 1319 females of all age groups ranging from 14 years to 85 years were analyzed for symptoms and risk factors for cervical cancer. The study variables included age, marital status, age at marriage, age at menarche, age at menopause, age at first childbirth, abortion, oral contraceptive pill (OCP) consumption, ovulation induction, hormone replacement, any breastfeeding, painful micturition, vaginal bleeding, rectal bleeding, vaginal discharge and regarding pain.

2.3. Statistical analysis

All scale variables were presented as mean \pm SD and categorical with respective proportions. Data of risk factors namely current age, age at marriage, age at menarche and age at menopause, etc. were analyzed to quantify the magnitude of association with the prevalence of common symptoms of

cervical cancer. 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).

3. Results

3.1. Characteristics of the study population

A total of 1319 females of all age group ranging from 14-85 years were screened for symptoms related to gynecological cancer at different health camps in the western parts of Uttar Pradesh and eastern Rajasthan. Background demographic and prevalence of symptoms related were presented in Table 1.

The prevalence of gynecological symptoms such as painful micturition was found to be 10.8% followed by white discharge per vagina (7.7%), pelvic pain (2.9%) and post coital bleeding/spotting per vagina (0.4%). The mean age of the females was 41.3 ± 14.1 years, and the majority of them were

married (86.3%). The average age at menarche was nearly fourteen years (13.8 ± 1.1 years), age at marriage was twenty years (19.9 ± 2.3 years), age at first childbirth was twenty-two years (22.2 ± 2.8 years), and age at menopause was forty-five years (45.4 ± 2.8 years). Out of the total participated women, more than fifty percent of eligible women were pregnant at least once (54.9%), having one living child (64.7%), and no abortions (85%) at the time of screening.

3.2. Association between factors and symptoms

The observed association between different symptoms and factor variables are depicted in Table 2. The prevalence of painful micturition, white discharge per vagina and pelvic pain in the age group 25–44 years was found to be 22.1%, 21% and 8% respectively and the distribution of symptoms was statistically associated ($p < 0.05$) with age. Married women had observed a higher number of cases with the symptoms as compared to unmarried/widow females. Prevalence of symptoms was reported to be higher among the females who married ≤ 20 years of their age, and the distribution was statistically significant ($p < 0.05$). The majority of females ($n = 1237$) started their menstruation cycle at 12–15 years of age. The painful micturition and pelvic pain were statistically related ($p < 0.05$) with the proportionate variation in menstruation cycle. Prevalence of symptoms was found to higher among the females having time interval between marriage and menarche less than five years (14.6% for painful micturition, 10.4% for white discharge per vagina and 4.7% for pelvic pain). Prevalence of symptoms was reported to be higher 13.6%, 11.3% and 5.3% for painful micturition, white discharge per vagina and pelvic pain respectively among the females who married in 18–20 years of their age. However, the prevalence of gynecological symptoms were not statistically related ($p > 0.05$) with the age of menopause.

The proportion of symptoms was found to be higher among the females who experienced one or two pregnancies, and it was statistically significant with painful micturition ($p < 0.001$) and white discharge per vagina ($p < 0.05$). Similarly, females with one or two living children were also showing a higher occurrence of symptoms and painful micturition ($p < 0.01$) and white discharge per vagina ($p < 0.01$) were associated with the prevalence. The preponderance of females (945 out of 1112 eligible women) was not undergone to any abortion. However, their distribution was not showing any association with the symptoms.

3.3. Independent risk factors

Further, the multivariable logistic regression was used to explore the independent risk factors for the occurrence of symptoms related to gynecological cancer. Table 3 shows the chances of developing painful micturition were significantly associated with age 45–54 years (AOR = 2.5; 95% C.I.: 1.4–4.5, $p = 0.01$), abnormal age for start of menstruation cycle (AOR = 5.1; 95% C.I.: 1.2–21.1, $p = 0.03$) and the females with two or more living children (AOR = 1.6; 95% C.I.: 1.1–2.5, $p = 0.01$) with respect to their reference category. Risk of occurrence of white discharge per vagina was statistically related to the different age groups as < 25 years (AOR = 6.4; 95%

Table 1 – Background profile of females screened for gynecological cancer.

Background variables	Number	%
Total female screened	1319 (100)	
Current age of females (years) (mean \pm SD)	41.3 \pm 14.1	
Age at marriage (years) (mean \pm SD)	19.9 \pm 2.3	
Age at menarche (years) (mean \pm SD)	13.8 \pm 1.1	
Age at menopause (years) (mean \pm SD)	45.4 \pm 2.8	
Age at first child birth (years) (mean \pm SD)	22.2 \pm 2.8	
Marital status		
Unmarried	122	9.2
Married	1138	86.3
Widow	59	4.5
Number of pregnancies among married and widow women (n = 1197)		
Non pregnant	85	7.1
One time	657	54.9
Two times	282	23.6
Three times	139	11.6
Four or more times	34	2.8
Number of women having living children (n = 1112)		
No child	77	6.9
One child	720	64.7
Two children	234	21.0
Three or more children	81	7.4
Number of women underwent abortions (n = 1112)		
No abortion	945	85.0
Single abortion	142	12.8
Two or more abortions	25	2.2
Symptoms for gynecological cancer		
Painful micturition	143	10.8
White discharge per vagina	101	7.7
Pelvic pain	38	2.9
Post coital bleeding/spotting per vagina	5	0.4

Table 2 – Comparison of different symptoms with risk factors of gynecological cancer.

Risk factor variables	Total	Symptoms for gynecological cancer related symptoms					
		Painful micturition (%)	p value	White discharge per vagina (%)	p value	Pelvic pain (%)	p value
Age group (years) (n = 1319)							
<25	144	13 (9.0)	0.020	17 (11.8)	0.001	5 (3.5)	0.025
25–34	275	30 (10.9)		35 (12.7)		14 (5.1)	
35–44	348	39 (11.2)		29 (8.3)		10 (2.9)	
45–54	261	41 (15.7)		10 (3.8)		7 (2.7)	
≥55	291	20 (6.9)		10 (3.4)		2 (0.7)	
Marital status (n = 1319)							
Unmarried	122	10 (8.2)	0.091	5 (4.1)	0.018	0	0.002
Married	1138	131 (11.5)		96 (8.4)		38 (3.3)	
Widow	59	2 (3.4)		0		0	
Age at marriage (years) (n = 1198)							
<18	146	24 (16.4)	0.088	17 (11.6)	0.001	9 (6.2)	0.005
18–20	655	74 (11.3)		65 (9.9)		25 (3.8)	
21–24	342	29 (8.5)		11 (3.2)		3 (0.9)	
≥25	55	6 (10.9)		3 (5.5)		1 (1.8)	
Age at menarche (years) (n = 1319)							
≤11	35	0	0.002	6 (17.1)	0.089	4 (11.4)	0.013
12–13	434	36 (8.3)		36 (8.3)		13 (3.0)	
14–15	803	105 (13.1)		54 (6.7)		18 (2.2)	
≥16	47	2 (4.3)		5 (10.6)		3 (6.4)	
Duration between age at marriage and menarche (years) (n = 1197)							
<5	364	53 (14.6)	0.042	38 (10.4)	0.101	17 (4.7)	0.072
5–9	706	67 (9.5)		51 (7.2)		20 (2.8)	
≥10	127	13 (10.2)		7 (5.5)		1 (0.8)	
Age at menopause (years) (n = 562)							
<45	205	30 (14.6)	0.051	11 (5.4)	0.248	3 (1.5)	0.843
≥45	357	33 (9.2)		12 (3.4)		6 (1.7)	
Age at first child birth (years) (n = 1159)							
18–20	398	54 (13.6)	0.143	45 (11.3)	0.002	21 (5.3)	0.001
21–24	514	58 (11.3)		40 (7.8)		15 (2.9)	
≥25	247	21 (8.5)		9 (3.6)		1 (0.4)	
Number of pregnancies among married and widow women (n = 1197)							
Non pregnant	85	0	0.001	2 (2.4)	0.033	1 (1.2)	0.231
One time	657	92 (14.0)		64 (9.7)		27 (4.1)	
Two times	282	26 (9.2)		16 (5.7)		5 (1.8)	
Three or more times	173	15 (8.7)		14 (8.1)		5 (2.9)	
Number of women having living child (n = 1112)							
No child	77	2 (2.6)	0.001	0	0.009	0	0.144
One child	720	104 (14.4)		66 (9.2)		28 (3.9)	
Two child	234	22 (9.4)		19 (8.1)		5 (2.1)	
Three or more child	81	5 (6.2)		9 (11.1)		4 (4.9)	
Number of women underwent abortions (n = 1112)							
No abortion	945	108 (11.4)	0.339	82 (8.7)	0.862	34 (3.6)	0.338
Single abortion	142	21 (14.8)		11 (7.7)		2 (1.4)	
Two or more abortions	25	4 (16.0)		1 (4.0)		1 (4.0)	

Bold values show either significant p values or category total.

C.I.: 2.4–16.9, $p = 0.02$), 25–34 years (AOR = 4.4; 95% C.I.: 2.0–9.5, $p = 0.03$) and 35–44 years (AOR = 2.6; 95% C.I.: 1.2–5.7, $p = 0.01$) with reference to age ≥ 55 years. It was also associated with the abnormal age of menarche (AOR = 2.0; 95% C.I.: 1.1–3.9, $p = 0.02$) as compared with the normal age of start (12–15 years). The likelihood of developing pelvic pain was significantly related to the females < 25 years (AOR = 8.4; 95% C.I.: 1.4–12.1, $p = 0.04$) and 25–34 years (AOR = 7.9; 95% C.I.: 1.7–8.3, $p = 0.03$) of their age. Pelvic pain was also independently

related to the abnormal age of menarche (≤ 11 or ≥ 16 years) (AOR = 3.6; 95% C.I.: 1.6–8.5, $p = 0.03$) concerning the standard age of start.

4. Discussion

Cervical cancer remained first out of the leading cancers among females in Indian Republic.¹⁷ Cervical cancer screening

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

Predictors of symptoms	Painful micturition		White discharge per vagina		Pelvic pain	
	AOR	95% C.I.	AOR	95% C.I.	AOR	95% C.I.
Age group (years)						
<25	1.2	0.4–3.5	6.4	2.4–16.9 ^a	8.4	1.4–12.1 ^a
25–34	1.6	0.9–3.1	4.4	2.0–9.5 ^a	7.9	1.7–8.3
35–44	1.6	0.9–2.9	2.6	1.2–5.7 ^a	4.0	0.8–19.6
45–54	2.5	1.4–4.5 ^a	1.1	0.4–2.2	4.1	0.8–20.7
≥55 [®]						
Marital status						
Unmarried/widow [®]						
Married	1.7	0.9–3.2	3.5	1.4–8.7	–	–
Age at marriage (years)						
<18	2.2	0.7–7.3	1.1	0.2–5.6	3.5	0.4–28.4
18–20	1.3	0.4–3.8	1.3	0.3–5.9	2.1	0.3–16.1
21–24	1.2	0.4–3.4	0.7	0.2–3.2	0.6	0.1–5.4
≥25 [®]						
Age at menarche (years)						
Normal age (12–15) [®]						
Beyond normal (≤11 or ≥16)	5.1	1.2–21.1 ^a	2.0	1.1–3.9 ^a	3.6	1.6–8.5 ^a
Duration between age at marriage and menarche (years)						
<5	1.5	0.8–2.9	1.8	0.8–4.1	5.5	0.7–42.3
5–9	0.9	0.5–1.8	1.3	0.6–2.9	3.6	0.5–27.2
≥10 [®]						
Age at 1st child birth (years)						
18–20	0.9	0.4–1.9	1.6	0.6–4.4	2.2	1.6–9.1 ^a
21–24	1.0	0.5–2.0	1.4	0.5–3.6	6.7	0.9–7.1
≥25 [®]						
Number of pregnancies among married and widow women						
Up to one [®]						
Two times	0.9	0.4–1.8	0.5	0.3–1.4	0.4	0.2–1.3
Three or more times	1.2	0.5–3.0	0.8	0.4–1.7	0.8	0.3–2.6
Number of women having living child						
Up to one [®]						
Two or more	1.6	1.1–2.5 ^a	1.1	0.7–1.8	0.8	0.4–1.7
Number of women underwent abortions						
No abortion [®]						
Single abortion	1.4	0.8–2.3	0.9	0.5–1.8	0.4	0.1–1.7
Two or more abortions	1.6	0.5–4.7	0.5	0.1–3.8	1.5	0.2–11.6

AOR: adjusted odds ratio; C.I.: confidence interval; [®]: reference category.

^a *p* value < 0.05.

is one of the easiest and effective methods for identification and prevention. The present study highlights the factors which influence the causal pathway between demographic, reproductive factors with increasing risk of cervical cancer.

The common symptoms related to cervical cancer reported in this study were painful micturition (10.8%) followed by white discharge per vagina (7.7%) and pelvic pain (2.9%). A hospital based study 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.¹⁸ The reported prevalence of these symptoms was lower than the study by Gupta et al. from the same region except for painful micturition.¹⁸ However, as per literature bleeding per vagina is a most common symptom but here we did not find any significant number. Differences in the occurrence of prevalence may be related to the relatively lesser sample size and

community/health camp based screening of the general population rather than a hospital.

In the present study, the observed peak proportion of various abnormalities was found to be in the reproductive age group (18–44 years). The age below 35 years was more at risk for developing white discharge per vagina and age group 25–44 years was at higher risk of complaining pelvic pain. However, painful micturition was observed more frequent in the age group 25–54 and post-menopausal age group (45–54 years) was independently related to the risk (AOR = 2.5) of painful micturition. These results are in similar with earlier studies.^{18,19} Although early marriage is not a risk factor for cervical cancer. A large prospective cohort study from rural South India reported that marital status and age at marriage both were not associated with the development of cervical cancer.¹⁹

The time interval between age at menarche and marriage was found to be a risk factor for cervical cancer in many studies.^{20,21} A study by Natphopsuk et al.²² 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 with ORs ranging from 3.32–4.09 and the respective adjusted OR range for the 4–5, and 2–3-year-old groups were 4.1 and 2.9. However, in the present study, the time interval between age at menarche and marriage showed no association in the multivariate regression analysis for the difference <5 years despite the high prevalence of symptoms may be due to small size.

The present cross-sectional study is also in agreement with those results. Age at marriage may be considered as a surrogate determination of age at first intercourse in the Indian scenario. Moreover, some case–control studies reported that convincing evidence of risk for cervical cancer associated with first sexual intercourse in an earlier age (<20 years).^{18,23,24} Stone et al. have also pointed out that first intercourse before reaching to age 15 years is a risk factor for cervical cancer.²⁵ Even despite the fact that age at marriage did not produce a significant association with symptoms, our estimated odds ratios in line with previously reported studies and it may be considered as a proxy measure of age at first sexual intercourse.

The abnormal age of menarche (≤ 11 or ≥ 16 years) was found to be a potential risk factor for the development of symptoms as painful micturition (AOR = 5.1, 95% C.I.: 1.2–21.1, $p = 0.03$), white discharge per vagina (AOR = 2, 95% C.I.: 1.1–3.9, $p = 0.02$) and pelvic pain (AOR = 3.6, 95% C.I.: 1.6–8.5, $p = 0.03$) in the present study that further increases the hazard of cancers including breast, epithelial ovarian cancer etc.^{26,27} other than cervical cancer. Therefore, it may be concluded that the unusual age of start of menstrual cycle could lead to increasing the risk of several types of cancer. In our study females having ≥ 2 children have approximately two fold risk (AOR = 1.6, 95% C. I.: 1.1–2.5, $p = 0.01$) of developing painful micturition.

Moreover, the number of pregnancies were not directly associated with the likelihood of developing symptoms. A case–control study from Chennai has also been showing the increase in the risk of cervical cancer (OR = 7.3) among HPV-positive women with more child births in comparison of less.²⁸ Multiparity might increase the risk of cervical cancer as pregnancy encouraged the cervical changes that lead to the development of cancer malignancy.²⁹

Nearly 4% females out of the onetime pregnant (26/657) and 12.8% females out of the two times pregnant (36/282) have been observed with no living child, and that was significantly related to the higher prevalence of symptoms ($p < 0.05$). Similarly, eighty-six out of the total females having one living child ($n = 720$) underwent abortions (64 one time and 12 two times), and it showed a significant relation with symptoms ($p < 0.05$). However, a total number of abortions were not significantly related to any symptoms in the multivariable analysis.

Other socio-demographic risk factors may be education, occupation and the family income of female as reported by Thulaseedharan et al.¹⁹ in their study among the rural population of southern India. However, these factors were not assessed in the present study.

Numerous other studies have also pinpointed the significance of socio-demographic, economic and reproductive factors in planning to control cervical cancer.^{8,19,30} Improving socioeconomic status and initiation of different screening techniques results in decline the cervical cancer incidence and mortality worldwide.³¹

5. Conclusion

The study has focused primarily on the prevalence of symptoms related to cervical cancer and its association with various demographic and reproductive risk factors among the screened women from the general population. Lack of awareness was also experienced during the screening about the key risk factors for cervical cancer among women that pointed out the issue of limited knowledge as reported by other studies. In this study, it was observed that higher age, abnormal age at menarche, early child bearing age and giving birth to two or more children might work as risk factors related to gynecological cancer-related symptoms.

6. 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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Ethical approval

The screening was conducted after obtaining ethical approval from the scientific advisory committee (SAC) of the Nayati Healthcare and Research Centre. This study follows the operational principles of the declaration of Helsinki and adheres to the Belmont report principles. The local health administrations of the selected area were also informed to provide the necessary help during the camp. Informed consent was obtained from the females came to the screening camp. The benefits and the purpose of screening were also informed in the local language.

Conflicts of interest

The authors have none to declare.

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