Original Research Article

A study to assess select risk factors for carcinoma cervix among patients attending Kidwai Memorial Institute of Oncology

Swapnajaswanth M.1*, Suryanarayana S. P.2, Suman G.3, Murthy N. S.3

Department of Community Medicine, 1Rajarajeswari Medical College, 2Ambedkar Medical College, 3M. S. Ramaiah Medical College, Bangalore, Karnataka, India

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*Correspondence:
Dr. Swapnajaswanth M.,
E-mail: swapnajaswanth@gmail.com

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ABSTRACT

Background: Cervical cancer is an important public health problem worldwide; it is second most common cancer among women aged 15-44 years globally (Globocan 2012). The objective of the study was to study the association between select risk factors and carcinoma cervix among patients attending Kidwai Memorial Institute of Oncology, Bangalore.

Methods: Hospital based case-control study was carried among newly diagnosed cases of cervical cancer, cases and apparently healthy controls were selected. Statistical analysis was performed using, Chi square test of significance, logistic regression were preformed.

Results: Univariate analysis revealed the following variables as significant risk factors these were Age at consummation of marriage <18 years OR 5.9 (2.6-19.4), Age 1st pregnancy <18 years OR 3.4 (2.2-5.2), live births delivered >5 OR 2.9 (1.7-5.8), marital status other than those who were married OR 1.7 (1.2-2.6), education of study subject being uneducated OR 3.9 (2.9-5.7), not washing genitals after sex OR 2.8 (1.6-4.9), material used during menstruation other than sanitary pads OR 6 (3.1-11.7), sex during menstruation OR 3 (1.1-7.9), not washing of private parts daily OR 10.8 (6.4-18.2), not taking bath daily OR 4.4 (2.8-7), open air defecation 7.6 (5.4-11.7), tobacco use OR 3.3 (2.2-5.6), never use of any contraceptive OR 3.7 (1.0-8.3) were significant at 0.05 level. Following backward multiple logistic regression analysis the following variables were independently associated with the development of cancer cervix, these were, age at 1st pregnancy <18 years OR 2.2 (1.2-3.8), use of material other than sanitary pads OR 3 (1.3-6.5), having sex during menstruation OR 4.3 (1.2-15), not washing of private parts daily OR 5.5 (2.9-10.4), open air defecation OR 2.6 (1.4-4.7), attained significance at 0.05 level.

Conclusions: The study has revealed that age at 1st pregnancy <18 years, use of material other than sanitary pads, having sex during menstruation, not washing of private parts daily, open air defecation, as an independent risk factor for the development of cancer cervix. It can be noted that all the risk factor mentioned above is highly amenable for primary prevention.

Keywords: Cancer cervix, Risk factors, Cases control study

INTRODUCTION

The burden of non-communicable disease is increasing due to increasing life expectancy, change in life style and behavioral pattern of people and improved medical care. The burden of cancer is distributed unequally between developed and developing countries, with particular cancer types exhibiting different patterns of distribution. According to WHO estimates for 2011, cancer now causes more deaths than all coronary heart disease or all stroke.1
Cervical cancer is the second most common female cancer in women aged 15 to 44 years and fourth most common cancer in women in the world, with an estimated 528,000 new cases and 266,000 deaths, accounting for 7.5% of all female cancer deaths in 2012 (Globocan, 2012). In developed countries Age-standardized Incidence and Mortality Rates is 9/100,000 and 3.2/100,000 for developing countries it is 15.7/100,000 and 8.3/100,000. More than 85% of these cases and deaths occur in developing countries where as in affluent countries, cancer cervix does not find place even in top five cancers in women. The disproportionately high burden of cervical cancer in developing countries and elsewhere in medically underserved populations is largely due to a lack of screening that allows detection of precancerous and early stage cervical cancer.

Cervical cancer ranks second among the female cancers in India. India bears one-third of the World’s burden of Cervical Cancer. The incidence of cervical cancer for the year 2012 in India was 123,000, and mortality was 67,000. The age standardized incidence rate for cancer cervix in India is 27/100,000 population and mortality rate being 15.2/100,000 and DALYs lost is 431,538. In Bangalore PBCR cancer cervix was the second leading site accounting for about 12.3% of cancer in females, leading site being Breast (27.5%). The age adjusted incidence rate for cancer cervix was 15.3/100000 population.

Risk factor for development of cervix cancer includes human papilloma virus (HPV) infection which has been established as the necessary, but not solely sufficient, cause of cervical cancer. Majority of women though infected with an oncogenic HPV type never develop cervical cancer, which suggests that additional factors acting in conjunction with HPV influence the risk of disease development, hence the objective of the study was to assess the association between select risk factor and cancer cervix among patient attending Kidwai Institute of Oncology.

METHODS

An age group matched case-control study was carried out at Kidwai Memorial Institute of Oncology, Bangalore, Karnataka, India from February 2011 to May 2012. The institutional Ethical clearance was obtained. Kidwai Memorial Institute of Oncology which is a Regional cancer centre for Karnataka. Necessary permission was sought from the concerned authorities in Kidwai Memorial Institute of oncology.

Cases were newly diagnosed and histologically confirmed cases of cervical cancer, above 30 years of age, attending Kidwai Memorial Institute of Oncology Bangalore. One control was selected for each case (1:1 ratio), the cases and controls were group matched for age (±5 years), and controls were apparently healthy hospital attendees (relatives, friends and other visitors).

Inclusion criteria

Histologically confirmed newly diagnosed cases of squamous cell carcinoma of cervix, above 30 years of age including all stages of the disease, who were willing to participate in the study. No previous treatment for any kind of malignancy.

Exclusion criteria

Patient diagnosed with other gynecological problems and cancers (i.e., vagina, vulva, cancer of endometrium, ovary and breast) adenocarcinoma of cervix, and individuals who are not able to respond coherently to the question asked. Controls were excluded if they had undergone hysterectomy.

Sample size was calculated using N master, the study by Silvia et al was used as reference to calculate sample size. Proportion of cases and controls with respect to age at 1st intercourse was taken, with alpha error of 10% and 80% power; the sample size was calculated to be 190 each for cases and controls.

A predesigned semi structured questionnaire was developed and pilot tested. The study subjects were selected from the Department of Radiotherapy, patients were informed about the study objectives and invited to participate, all cases were histologically confirmed and then included in study, and informed written consent was taken from both the cases and controls. Semi-structured questionnaire was administered to both cases and controls and information regarding the socio-demographic factors, reproductive and sexual history, smoking and hygiene were collected.

Statistical analysis

The data was entered in excel and analysis was done using SPSS software version 18.0, all the quantitative variable such as age, parity etc, is summarized in terms of mean, median, etc; to understand the variation with the quantitative variable standard deviation is calculated. The strength of association for various risk factors between cases and controls was estimated using odds ratio with 95% confidence interval and p<0.05 was considered for statistical significance. To evaluate the independent risk factor associated with the development of carcinoma cervix, backward multiple logistic regression analysis was performed.

RESULTS

The study included 200 cases of cancer cervix and equal number of apparently healthy controls.

Medical information

All the cases were squamous cell carcinoma of cervix. Among the cases 109(49.5%) of them presented to...
hospital in stage III followed by 79(39.5%) presented in Stage II. Only 5 (1.2%) of the study subjects had a knowledge with respect to Pap smear and only 2 of them had undergone Pap test as a screening procedure in their lifetime.

Table 1: Socio demographic profile of the study subjects.

| Socio demographic factor | Cases (%) n=200 | Controls (%) n=200 |
|--------------------------|----------------|-------------------|
| Residence                |                |                   |
| Rural                    | 121 (60.5)     | 48 (24)           |
| Urban                    | 79 (39.5)      | 152 (76)          |
| Education                |                |                   |
| Not literate             | 139 (69.5)     | 73 (36.5)         |
| Literate                 | 61 (30.5)      | 127 (63.5)        |
| Religion                 |                |                   |
| Hindu                    | 190 (95)       | 184 (92)          |
| Others                   | 10 (5)         | 16 (8)            |
| Marital Status           |                |                   |
| Married                  | 131 (65.5)     | 154 (77)          |
| Widow, separated         | 69 (34.5)      | 46 (23)           |
| Age at marriage          |                |                   |
| <18years                 | 163 (81.5)     | 131 (65.5)        |
| >18years                 | 37 (18.5)      | 69 (34.5)         |
| S.E.S as per BG prasad’s classification | | |
| Upper high class         | 30 (15)        | 101 (50.5)        |
| High class               | 57 (28.5)      | 56 (28)           |
| Upper middle class       | 67 (33.5)      | 27 (13.5)         |
| Lower middle class       | 35 (17.5)      | 14 (7)            |
| poor                     | 11 (5.5)       | 2 (1)             |

Table 2: Univariate and multiple logistic regression analysis for select risk factors for cancer cervix.

| Variables                                | Levels | Cases No. | Controls No. | Univariate OR | Multivariate OR |
|-------------------------------------------|--------|-----------|--------------|---------------|-----------------|
| Education of study subject                | Not literate | 139 | 73 | 3.9 (2.9-5.7) | 0.0001 | 1.3 (0.63-2.9) | 0.433 |
|                                           | Literate | 61 | 27 | 1 | 1 | 1 |
| Marital status                           | Others | 69 | 46 | 1.76 (1.2-2.6) | 0.011 | 1.3 (0.76-2.4) | 0.298 |
|                                           | Married | 131 | 154 | 1 | 1 | 1 |
| Age at consummation of marriage           | <18 years | 162 | 129 | 5.9 (2.61-19.44) | 0.0003 | 2.7 (1.41-41.1) | 0.36 |
|                                           | ≥18 years | 38 | 71 | 1 | 1 | 1 |
| Age at 1st Pregnancy                      | <18 years | 92 | 35 | 3.8 (2.8-5.9) | 0.0001 | 2.2 (1.2-3.8) | 0.006 |
|                                           | ≥18 years | 107 | 161 | 1 | 1 | 1 |
| Live births delivered                     | >5 | 29 | 11 | 2.9 (1.7-5.8) | 0.0021 | 1.6 (0.6-4.1) | 0.256 |
|                                           | ≤5 | 171 | 189 | 1 | 1 | 1 |
| Washing genitals after sex                | Never | 179 | 150 | 2.8 (1.6-4.9) | 0.0001 | 1.4 (0.72-2.8) | 0.29 |
|                                           | Always | 21 | 50 | 1 | 1 | 1 |
| Material used during menstrual cycle      | Cloth | 188 | 144 | 6 (3.1-11.7) | 0.001 | 3 (1.3-6.5) | 0.005 |
|                                           | Pads | 12 | 56 | 1 | 1 | 1 |
| Sex during menstruation                   | Sometimes | 17 | 6 | 3 (1.15-7.9) | 0.018 | 4.3 (1.2-15.1) | 0.019 |
|                                           | Never | 183 | 194 | 1 | 1 | 1 |
| Washing of private parts daily            | No | 117 | 23 | 10.8 (6.4-18.2) | 0.0001 | 5.5 (2.9-10.4) | 0.001 |
|                                           | Yes | 83 | 177 | 1 | 1 | 1 |
| Taking bath daily                         | No | 99 | 36 | 4.46 (2.8-7.0) | 0.0001 | 1.004 (0.5-1.9) | 0.990 |
|                                           | Yes | 101 | 164 | 1 | 1 | 1 |
| Toilet                                    | Open air | 117 | 31 | 7.6 (5.4-11.7) | 0.001 | 2.6 (1.4-4.7) | 0.001 |
|                                           | Toilets | 83 | 169 | 1 | 1 | 1 |
| Tobacco use in all forms >6months         | Yes | 52 | 19 | 3.3 (2.2-5.6) | 0.0001 | 1.09 (0.51-2.3) | 0.811 |
|                                           | No | 148 | 181 | 1 | 1 | 1 |
| Oral contraceptive use >6months           | Never used | 192 | 173 | 3.7 (2-8.3) | 0.0006 | 1.6 (0.55-4.7) | 0.37 |
|                                           | used | 8 | 27 | 1 | 1 | 1 |

Table 1 depicts the socio demographic profile of the study subjects. The mean age of the study subjects was 48years (S.D±9.31 years) the age range of the study subjects was from 30-70 years. Most of the study subjects
were married, 121 (60.5%) of the cases were from rural area, majority of the study subjects were Hindus, 67 (33.5%) of the cases belonged to upper middle class according BG Prasad’s classification of socioeconomic status and 139 (70%) of the cases were not literate. Mean age at marriage of the study group 17.34 years, S.D ±3.39, majority of the study subjects age at marriage was less than 18years (73.5%). Among cases 163 (81.5%) of them were married before the age of 18years as compared to 131 (65.5%) among controls. Among the cases 92 (46.2%) of them were 1st time pregnant <18years of age as compared to only 35 (18%) of the controls.

The univariate odds ratio and corresponding 95% CIs for cancer cervix according to various risk factors are shown in Table 2. Not literate (OR vs. literate=3.9), risk among widows, separated and divorced women (OR vs. currently married women =1.76)

The influence of reproductive and menstrual factors revealed the following, an increased risk of cancer cervix was also found with Age at consummation of Marriage <18 years (OR vs. ≥18 years=5.9), age at 1st pregnancy <18 years (OR vs. ≥18 years=3.8), women who reported more than 5 births had a higher risk (OR vs. ≤5 =2.9), sex during menstruation (OR=3), not using any method of contraception (OR=3.7)

Lack of hygiene showed an increase with cervical cancer, which included not taking bath daily (OR=4.46), lack of toilet (OR=7.6) not washing of private parts daily (OR=10.8), use of cloth during menstruation (OR vs pads =6) and use of tobacco in various forms had a risk (OR=3.3).

Results of multiple logistic regression revealed the following variables to be independently associated with cancer cervix these are age 1st pregnancy <18years, material used during menstruation (cloth), sex during menstruation, not washing of private parts daily, open air defecation.

**DISCUSSION**

This is one of the few case-control study on cancer cervix from Karnataka. This study was conducted at a Kidwai Memorial Institute of Oncology, which are both a Hospital Based Cancer registry and population based cancer registry.

In this study the majority 146 (36.5%) of the cases belonged to the age group ranging from 41 to 50 years, this reveals that the productive age group is affected. In India the peak age for cancer cervix is 45 to 54 years similar finding were found in studies done by Francheschi et al in Chennai and by Biswas et al among Rural Indian women.6-8 The education status among the groups were compared it was seen that the 139 (69.5%) of the cases were not literate compared to 73 (36.5%) of controls, the odds of cancer cervix was 3.9 folds (95% C.I 2.9-5.7) more among the not literate compared to literate, which was statistically significant similar results were found in study done in Chennai with odds of 4.8 for cervical cancer (illiterate vs. literate) and other studies.6,9-12 In a metaanalysis by Parikh et al it was found that non literate women were at higher risk of cervical cancer.13

**Marital status and reproductive factors**

In this study the married subjects were compared with widow, separated and divorced and these are mentioned as others, the odds of cancer cervix was 1.7 (95% C.I 1.2-2.6) times higher among others as compared to married subjects, that was statistically significant, similar finding were found in Francheschi et al study done in Chennai, the odds was 8.3 (95% C.I 4.2-17.6) for widowed.6,14

Age at consummation of marriage, (<18 years vs. ≥18 years) the odds was 5.9 times (95% C.I 2.6-19.4) more among women less than 18 years which was statistically significant, similar finding were found in Biswas et al, a meta-analysis also revealed the similar findings.6,8,15

Age at 1st pregnancy, among the cases 92 (46.2%) and controls 35 (18%) were 1st time pregnant less than 18 years of age, the odds was 3.9 (95% C.I 2.8-5.9) time more among those who had 1st pregnancy (<18 years vs. ≥18 years) that was statistically significant. A study in Chennai reported the odds of cancer cervix was 1.1, 2.2 respectively for age at pregnancy at 17-18 years and <17 years as compared to >18 years, a meta-analysis also revealed similar results.6,16,17

Number of live births was considered as one of the risk factor and analysed, the study showed odds of 2.9 (95% C.I 1.7-5.8) time more risk of cancer cervix among women with >5 live births compared to 0-5 live births, statistically significance obtained. A hospital study showed odds of 5.7 compared to 1-2 births, similar results were also found in other studies.6,16,18,19

**Genital and menstrual hygiene**

**Material used during menstruation**

This study revealed that still many study subjects 332 (83%) used cloth as material during their menstruation. Among case 188 (94%) used cloth compared to 144 (72%) among controls, the odds of cancer cervix was six folds higher among cloth users compared to those using sanitary pads (95% C.I 3.1-11.7) and that was statistically significant. Study by Chaouki et al and Zhang et al. Reported use of sanitary pads had odds of 0.36 (0.13-0.95) and 0.3 respectively as compared to not using sanitary pad.20,21

**Sex during menstruation**

Most of the study subjects did not practice sex during menstruation, the odd of cancer cervix was 3 folds higher.
(95% C.I 1.1-7.9) among those who occasionally had sex during menstruation compared to those who did not have sex during that period, a study by Sichuan et al revealed that there was a strong protection in women who abstained from sexual intercourse during the menses.  

Washing of private parts daily during bathing and/or after toilet was asked: the odds of cancer cervix was 10.8 (95% C.I 6.4-18.2) folds higher among those who did not wash their private parts daily compared to those who washed daily. Similar result are obtained in study by Zhang et al with odds of 4.8 for absence of daily genital washing and study by Peng et al demonstrated a strong protection in women who washed genital area as compared to who did not wash.  

Toilet usage vs. open air defecation the odds of cancer cervix was 7.6 times more among open air defecators, study by Franceschi et al showed odds of 4.8 for those who did not have toilet at home.  

Tobacco use  

The odds of cancer cervix was 3.4 (95% C.I 2.2-5.6) times for those who consumed tobacco of any form compared to those who did not use, similar results are shown in a study done in Philippines, Thailand and Utah.  

The factors which showed statistical significance at p≤0.05 in univariate analysis were considered for multiple logistic regression to check for independent association, which revealed factors like that early age at pregnancy, poor menstrual and genital hygiene as risk factors for cancer cervix.  

CONCLUSION  

The data shows that early pregnancy, poor menstrual and genital hygiene as risk factors for cancer cervix, and the above mentioned risk factors are highly amenable for primary prevention.  

Limitations  

- Investigator bias: could not be eliminated completely as the investigator was not blinded to the cases and controls, but the time duration for interviewing both the case and control has been same.  
- Referral Bias: The cases and controls were selected from a single hospital but the hospital where the study was carried out is comprehensive and regional center for cancer research and treatment in Karnataka. Patients from all over Karnataka as well as from adjoining areas of the neighboring states and other regions attended the hospital.  
- In this study cases and controls were not tested for HPV, however this would not pose a problem as HPV as already been considered as the necessary cause, hence other risk factors have been analyzed in this study.  
- In this study controls were not confirmed by any diagnostic test for not having cancer cervix, however only apparently healthy females were included, without any history of any prior or present gynecological problem.  
- The conformation for the presence of Sexually transmitted disease was done on the basis of syndromic approach alone without any investigations.  

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