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ORIGINAL ARTICLE

Changing Trends in the Epidemiology of Cervical Cancer in Upper Middle Class Women

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ABSTRACT

Introduction: Changing trends in the epidemiology of cervical cancer are reported from developing countries, but the new factors are not well documented, especially socioeconomic (SE) status.

Aim: To study the prevalence and factors associated with cervical cancer in upper middle SE class women from a tertiary care hospital in Chennai, South India.

Materials and methods: This is a case–control study of cases with cervical cancer and twice the number of asymptomatic controls, among women who underwent papanicolaou (PAP) smear test during 2009 to 2015.

Results: Of the 3,536 PAP smears examined, 48 (1.36%) had cervical cancer and 96 age- and year-matched controls were selected for the cases. The mean (± standard deviation, SD) age of cases was 51.3 (± 12.7) years and controls was 51.7 (± 12.7) years (p not significant, NS). Over 90% of both groups underwent surgical sterilization and had long married lives. The median parity of cases and controls was 2. Parity was 3 or more in 22 (44.9%), compared with 27 (28.1%) in controls ($p < 0.05$; relative risk, RR: 1.6 and 95% confidence interval, CI: 1.3–1.9). Among all the cases, 23 (48.0%) were asymptomatic. More than half, 28 (58.3%), of the cases and 50 (52.1%) of the controls had attained menopause (p = NS). About 7 (25%) of these cases reported postmenopausal bleeding (PNB).

Conclusion: Among the PAP smears tested, high prevalence (1.36%) of cervical cancer was noted. The associated factors were age >50 years, median parity of 2, history of PNB, and a long duration of sexual exposure. Nearly half the cases were asymptomatic, highlighting the need for routine screening of all postmenopausal women.

Keywords: Cervical cancer, Postmenopausal bleeding, Postparity, Socioeconomic status.

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INTRODUCTION

Worldwide, cervical cancer is the fourth most common cancer among women and second most common one in developing countries.[1] There are about 5.3 million new cases occurring annually worldwide, and this contributes to 7.5% of female cancer deaths.[1] In recent decade, cervical cancer is reported to be one of the leading causes of morbidity and mortality in women in India.[2] An estimate of 0.1 to 0.13 million new cases are being reported from India annually.[2] The disease burden of cervical cancer is enormous, with India alone contributing to 23% of the global figures.[3,4] Although recent studies have quoted a decrease in the trends of prevalence of cervical cancer, it is still a major problem in India.[5] Multiple factors such as age at marriage, parity, and poor vaginal hygiene have been found to increase the risk of cervical cancer in lower SE stratum.[5] However, similar prevalence and factors associated thereof have not been reported exclusively in Indian women hailing from higher and upper middle SE classes. This may be due to very few studies in this section of the women, with studies on cancer cervix concentrating on women from lower SE stratum. Also, changing trends in age at onset, influence of menopause, and effects of sterilization on the prevalence of cervical cancer have not been reported adequately.[5-8]

Our study was conducted to determine the prevalence of cervical cancer among women from the upper and upper middle SE classes undergoing preventive PAP smear test. The changing trends in factors affecting cervical cancer and the newly emerging factors, among this SE class, were our areas of interest. This study was done in a corporate hospital that caters to women predominantly from the upper and upper middle SE classes.

MATERIALS AND METHODS

A case control study was done among women undergoing PAP smear[9] for screening and diagnostic purposes

in Global Health City Hospital in Chennai, South India. Retrospective data were collected from case sheets of all women aged 15 to 75 years, who underwent PAP smears anytime from September 2009 to December 2014. These women presented either as outpatients for some gynecological or medical condition or had a master health check-up (screening with PAP smear for cervical cancer) in this hospital. All women diagnosed to be having a positive PAP smear for cervical cancer (confirmed by cervical biopsy in doubtful ones) were the "cases" for this study. Two PAP smear-tested women, with normal report, matched for age (± 5 years) and year of testing were selected as "controls" for each case. Data were collected on basic demographic characteristics, parity, gynecological and obstetric history, duration of illness, comorbidity diagnosed by clinical, laboratory, and radiological findings, family history of cervical cancer, and results of PAP smear/cervical biopsy. Data were collected by one of the coauthors (VS) by transcription from the case records.

STATISTICAL ANALYSIS

Data were analyzed using statistical package for the social sciences version 20. Statistical tests used were proportion test, Chi-square for proportions, analysis of variance (ANOVA) for means, Mann–Whitney U test for medians, and multivariate analysis for factors significant in proportions test. Numerical factors were converted to categorical variables for the purpose of multivariate analysis. A p value of less than 0.05 was considered significant.

The study was approved by the Ethical Committee of Gleneagles Global Health City Hospital, Chennai, India.

RESULTS

A total of 3,536 PAP smears were examined in the study center between 2009 and 2014 (Table 1). Of these, 2394 (67.7%) smears were normal and rest abnormal. Atrophic smears were 6.2% (218), inflammatory smears formed 21.4% (760), cancers of the reproductive organs or breast 1.7% (59), and 1.36% (48) were cases of cervical cancer. The rest of the women (3.0%) had other gynecological conditions.

Table 1 also shows the distribution of cases by the various years of PAP smear testing. Of the total smears tested, 1142 (32.3%) had one or the other abnormality. The overall prevalence of cervical cancer was 1.67% (95% CI: 1.62–1.72%). The prevalence was high in 2009 at 4.38% compared with a low of 0.94% in 2012 and a gradual rise in the subsequent years to 1.40 in 2014. A similar pattern was seen in proportion of cervical cancer among cases with abnormal PAP smears.

The mean age of the cases was 51.3 (± 12.7) years and that of the controls was 51.7 (± 12.7; *p* not significant). A total of 28 (58.0%) of the cases were above 50 years and only 7 (14.6%) were below 40 years. Over 90 percent of the cases and controls (91.8% and 94.6%, respectively) had undergone surgical sterilization. All the cases and controls were married, had single sexual partner, were nonsmokers, marked absence of vaginal douching was noted, and condoms were not being used after surgical tubal ligation.

Table 2 shows the parity of both cases and controls. Twenty two (44.9%) of the cases had a parity of more than 2, while only 27 (28.1%) of the controls were so (proportion test $p < 0.05$). The median parity of both cases and controls although was 2, proportion among cases with parity 3 or more was significantly higher at 44.9% (n = 22) compared with controls at 28.1% (n = 27) and with a moderate raised risk of 1.6 times (Chi-square $p < 0.05$; RR 1.6 and 95% CI: 1.3–1.9). Two of the cervical cancer cases had also received treatment for breast cancer earlier. More than half of the cases (28–58.3%) had attained menopause; among the controls, a similar proportion (50–2.1%) were so (*p* not significant) and hence, attainment of menopause did not reduce the risk of carcinoma cervix. Over half, i.e., 52.1% (25), of the cases reported to have had one or the other comorbidity; while 69.8% (67) of the controls were patients with other illnesses (being hospital controls) as seen in Table 2. None of the women, either cases or controls, reported multiple sexual partners.

As seen in Table 2, the commonest comorbidity was diabetes and/or hypertension in both cases and controls. Controls had similar proportions of comorbidity as the cases. Three-fourths (36–75.0%) of the cases had associated clinical conditions other than cervical cancer. A similar proportion of the controls (73–76.0%) also had some illness (*p* not significant) indicating that associated

Table 1: Distribution of women tested for PAP smear and cervical cancers detected

		Abnormal PAP smears		*Percentage of cases*	
Date of registration	*Total PAP done*	*No.*	*Cases*	*To total smears*	*To abnormal smears*
2009	120	23	7	4.38	3.04
2010	229	32	3	3.06	2.19
2011	644	101	12	2.33	1.49
2012	637	134	5	0.94	4.48
2013	938	471	8	1.17	2.34
2014	928	381	13	1.4	3.41
Total	3536	1142	48	1.67* (95% CI: 1.62–1.72)	5.17* (95% CI: 4.61–5.46)

Table 2: Demographic, fertility characteristics, and comorbidity

Characteristic	*Cases (n = 48)*	*Controls (n = 96)*	*Chi-square*/ANOVA**/ MW test*** p value*
Age in years: mean (±SD)	51.3 (± 12.3)	51.7 (± 12.7)	NS (0.98)**
Parity			
Median (range)	2 (0–9)	2 (0–8)	NS (1.0)***
2 or less—no. (%)	27 (55.1%)	69 (71.9%)	<0.05*
3 or more—no. (%)	22 (44.9%)	27 (28.1%)	
Comorbidity (chronic)			
Nil	23 (47.9%)	29 (30.2%)	<0.05*
Diabetes mellitus type II	14 (29.2%)	26 (27.1%)	NS (0.3)*
Hypertension	13 (27.1%)	27 (28.1%)	NS (0.6)*
Hypothyroid	3 (6.3%)	14 (14.6%)	NS (0.14)*
Cardio or cerebrovascular illnesses	4 (8.3%)	5 (5.2%)	NS (0.58)*
Kidney related carcinoma breast			
Bone and joint conditions	3 (6.3%)	1 (1.0%)	NS (0.07)
Others	2 (4.2%)	5 (5.2%)	NS (0.07)
	2 (4.2%)	6 (6.3%)	NS (0.61)
	13 (27.1%)	29 (31.2%)	NS (0.38)

*Of the four with a negative pap smear, two were positive clinically suspicious with subsequent smear taken elsewhere as positive and two others positive in cervical biopsy; **Four cases had normal cervical biopsy finding although their PAP smear showed evidence of squamous cell carcinoma; NS, Not significant; ***MW test used

Table 3: Other associated illnesses among cases and controls

PAP smear findings	*Case*	*Control*	*Cervical biopsy findings*	*Case*	*Control*
Normal	4	87	Normal	4	29
Atrophic	0	7	Inflammatory	3	0
Atro and inflammatory	0	1	Positive for malignancy	14	0
Inflammatory	1	0	Reactive smear	3	1
Positive for malignancy	42	0	Carcinoma *in situ*	2	0
ASCUS	1	0			

ASCUS, Atypical squamous cells of undetermined significance

illnesses were not a significant factor for cervical cancer. The common associated illnesses among the cases were hypertension in 10 women (20.8%) and diabetes mellitus in 5 (10.4%); other gynecological conditions such as cervicitis/vaginitis/erosion, endometriosis, fibroid uterus, and Bartholin's cyst were present in 4 (8.3%) cases. The proportion of other similar gynecological conditions among the controls was significantly higher with 22 cases (22.9% and $p < 0.05$).

Table 3 shows the presenting symptoms of the cases at the time of diagnosis. Of the 48 cervical cancer cases, only 25 (52.0%) were symptomatic. The remaining 23 cases, all asymptomatic, were positive either by PAP smear (22–45.8%) or by cervical smear (1–2.1%). Another 18 (37.6%) had cervicitis and/or vaginitis with or without dysfunctional uterine bleeding (DUB) and a positive PAP smear. Only two had erosion cervix with a clinical suspicion of cervical cancer (as against 13–13.5% in the controls), and the rest had other gynecological symptoms with a positive smear. One case also had ovarian cancer in addition to cervical cancer. Four cases had both cervical cancer and cancer of the left breast. None of the breast/ovarian cancers were squamous cell carcinoma, thus ruling out the chance of metastasis in the breast. In contrast, 60 (62.5%) of the controls were asymptomatic and had presented to the hospital for a master health check-up; rest of the controls either presented for cervicitis and/or vaginitis with or without DUB (13.5%) or erosion cervix (13.5%), and less than 5% each for prolapse uterus or pelvic infection or for ectropion with DUB. Thus, only 60 (62.5%) controls were asymptomatic ($p < 0.05$) in contrast to 36 (37.5%) who were symptomatic, and had presented to the hospital for a master health check-up; rest of the controls either presented for cervicitis and/or vaginitis with or without DUB or erosion cervix (13–13.5%) each, and less than 5% each for prolapse uterus or pelvic infection or for ectropion with DUB. Most of the cases (28–58.3%) had attained menopause and 7 of them, i.e., 25% reported post-PNB. Among the controls, although 59.4% (57) had attained menopause, only 3 of 57 (5.2%) had PNB ($p < 0.01$). The RR of PNB for cancer cervix in cases was significantly higher at 4.96 (95% CI: 1.40–17.56). The cases accidentally diagnosed formed 0.65% of the total PAP smears tested and nearly 1% (0.96%) of the abnormal smears indicating

Table 4: PAP smear and cervical biopsy findings of cases and controls

Clinical diagnosis	*Case*	*Control*	*Chi-square p-value*
Nil	12 (25.0%)	23 (24.0%)	0.9 (NS)
Diabetes mellitus	5 (10.4%)	17 (17.7%)	0.25 (NS)
Hypertension	10 (20.8%)	11 (11.4%)	0.13 (NS)
CAD/CVA	2 (4.1%)	0	<0.05
Other gynecological conditions	4 (8.3%)	22 (22.9%)	<0.05
Breast condition	3 (6.3%)	6 (6.3%)	1.0 (NS)
Kidney and urinary tract conditions	2 (4.2%)	5 (5.2%)	0.78 (NS)
Bone and joint conditions	1 (2.1%)	9 (9.4%)	0.10 (NS)
Others	8 (16.7%)	28 (29.2%)	0.10 (NS)

CAD, coronary artery disease; CVA, cerebrovascular accident; NS, not significant

Table 5: Effect of PNB and parity on cervical cancer

Parity	*PNB*	*Cases*	*Control*	*Chi-square p value*	*RR (95% CI)*
Less than 3	Yes	4	0	<0.001	24 (1.4–419.5)
	No	10	39		
3 or more	Yes	3	3	NS (0.79)	1.2 (0.3–4.7)
	No	7	9		

that the prevalence of asymptomatic cervical cancer is as high as 1% of the abnormal smears.

Table 4 shows the PAP smear and cervical biopsy findings of cases and controls. Of the 48 cases, 43 (89.6%) had a positive PAP smear with squamous cell carcinoma. Four (18.3%) had a negative smear and one an inflammatory smear. Of these five, three cases were positive on cervical biopsy and two others were clinically highly suspicious for cervical cancer and a tissue biopsy following (preventive) total abdominal hysterectomy showed evidence of squamous cell carcinoma, confirming presence of cervical cancer in all 48 cases. None of the controls had a positive PAP smear for cervical cancer, nor a clinical suspicion of the disease, although 13.5% had inflammatory smears. Three factors that were significantly associated with cervical cancer were age above 50 years with 58% of the cases above 50 years (95% CI for proportion 44–72%), parity 3 or more, and a history of PNB with 7 (14.6%) women having cancer cervix as against 3 (3,1%) controls. The RR for parity 3 or more was 1.77 (95% CI: 1.14–2.75) and that for PNB was 4.96 (95% CI: 1.40–17.56), thus illustrating the huge role played by PNB. A bivariate analysis was done for the effect of parity and PNB (Table 5), which showed the role of PNB in lower parity women of less than three to be significant and having a higher risk ($p < 0.001$ and RR 24.0 with 95% CI as 1.4–419.5) compared with those with higher parity. Thus, age and history of PNB in women above 50 years emerged as a major risk factor for cervical cancer in our study and not high parity.

DISCUSSION

In our study group, the cases of cancer cervix had a lower average parity of 2, and this finding is in contrast to that reported in other studies.[10,11] Mhaske et al[10] have reported a parity of 4 in 26.3% of their study on risk factors and cervical dysplasia/cancer; Dutta et al[11] have reported a higher odds ratio of human papillomavirus (HPV) detection in women with parity 4 or more without cancer cervix. The lack of parity as a risk factor in our study could be due to our cohort of women belonging to the higher SE group and literacy and, therefore, adoption of contraceptive methods at a younger age and lower parity. As per National Family Heath Survey (NFHS) 4 reports in the year 2015 to 2016, 49.4% of married women in the age group of 15 to 49 have undergone surgical tubal ligation in Tamil Nadu, South India.[12] Our study population (from a high SE group and literacy) had a higher rate of adoption of family planning methods (91.8%) even during the 1990s. Role of SE status as a risk factor has been documented by Centers for Disease Control and Prevention (CDC), Atlanta. However, they report cancer of the cervix as a disease of lower SE status women, since they are likely to have risky sexual activities like unprotected sex and sex with multiple partners, which can make a person more likely to get HPV, the most common cause of cervical cancer.[13] Our findings differ from that of CDC, Atlanta, in that we have been able to pick up prevalence rates as high as 1.36% of this cancer in high SE women with lower parity.

Cervical cancer has been reported to be a disease of the lower SE class, with 94% of the patients belonging to social classes 3 and 4, while the rest 6% belonged to social class 2, with no cases being reported in social class 1 (5). Similar observations have been made in several other countries including Britain by Gakidou et al.[14] with rates reported at 4.4% patients in SE class 1, 11.1% in class 2, 65.3% in class 3, 10.1% in class 4, and 9.1% in class 5.

However, in our study on upper and upper middle SE classes, the prevalence was 1.36%, although low, nevertheless present.

In our study group, we find that average age of occurrence of the disease was 51 years. Other studies have shown that cervical cancer is common among women in the age group 30 to 39 years in China and the United Kingdom and is the second most common cancer in women aged 15 to 44 years.[5,15] Average age at occurrence in our study group (51.3 years) was at least one decade more than that reported in the high-risk group of other studies. This could be due to a prolonged period of sexual exposure observed in our study group, with the median age at marriage in this cohort as 19.4 years (1980–90 cohort for age at marriage) as per national figures reported for all SE classes in the NFHS data.[12] Brock et al.[16] have also reported a higher risk of 4.5 for women with two to three sexual partners and at 8.1 for those with seven or more partners when compared with the risk for women with one or zero partners.[11] In our study, the cases have all reported of having only one sexual partner throughout their reproductive period, although most of them have had a prolonged married life. The prolonged sexual exposure resulting in cervical cancer has been reported by Lawson et al.[17] to be due to the effect of the excess mucus secreted by the mucus-bearing cells that gets dissolved by alkalis in the cervical mucosa, and then precipitated by acids from the vaginal mucosa.[18] This is reported to result in removal of the surface mucosa, thus causing cervical trauma leading to the proliferative and hyperplastic changes. Single sexual partner and absence of smoking are noted findings in our study group. There was marked absence of vaginal douching. Condoms were reported as not being used after surgical tubal ligation. Majority of the partners were not circumcised. Good vaginal hygiene,[19] regular usage of condoms, and universal circumcision for men can prove to be an effective tool to largely reduce the risk of cervical cancer in this group. Thus, probably poor sexual hygiene was a contributory factor in our cohort.

Crissman et al.[20] have reported a higher incidence of cancer of the endometrium in women aged 40 years or younger with PNB. Most of the other studies have not reported on the risk of PNB as a marker for cervical cancer.[3,4,6,7] In our study, women presenting with PNB had a very high risk (RR of 4.96 and 95% CI: 1.40–17.56), indicating that as the warning signal for cervical cancer; all such women should be compulsorily screened for cervical cancer with a cervical biopsy offered to them.

A low screening rate for cervical cancer has been reported among the poor women in countries such as Brazil, China, Germany, and India, with rates ranging from 5 to 22% in poor.[14] In our country, although the government has taken efforts to popularize cervical screening programs, the taking up rate is very poor as reported in the large-scale epidemiological study by Sreedevi et al.[5] In our study, more than half the cases with cervical cancer—25 (52%)—were symptomatic, and the rest half were picked up in an asymptomatic phase. This finding highlights the importance of regular PAP smear testing in any woman aged beyond the reproductive phase of life, irrespective of SE status or number of sexual partners. In addition, all women with PNB should undergo a frequent PAP smear testing (at least once in a year) to crop early cases of cancer cervix.

The study is a comprehensive one in that it has been conducted on all upper middle SE groups of women in the last 6 years reporting to our hospital for PAP smear as a screening measure. Thus, every case of cervical cancer was picked up by either smear or cervical biopsy. Although our study has confirmed some of the risk factors reported earlier, the newer ones observed were PNB and a low parity. If the present trend of low screening rates for cervical cancer continues to be influenced by the changing epidemiological trend of shift in age at marriage, SE status, and younger age at adoption of tubal ligation, the disease will no longer have an influence by all conventional risk factors, but have a different set of risk factors. This necessitates screening of postmenopausal women belonging to all SE status for detection of cancer cervix and followed by advice regarding lifestyle changes, especially related to sexual behavior. The above steps need to be added in the present cancer cervix control program.

Other interesting findings in our study were a concurrent occurrence of carcinoma breast in four cases and cancer ovary in one case along with cervical cancer. None of the breast/ovarian cancers were found to be squamous cell carcinoma, thus ruling out the chance of metastasis. This could be attributed as a part of the decadal shift in the patterns of concurrent occurrence of multiple cancers in different sites. Similar coexistent carcinomas have not been reported in the literature in this part of the world.

The major limitation in our study was the absence of data on age at sterilization and presence of sexually transmitted diseases that could have influenced our prevalence rates. The large confidence intervals for the RR in multivariate analysis were due to the low prevalence rates of cervical cancer in this cohort.

CONCLUSION

This study showed a high prevalence of cervical cancer even in older women above 50 years belonging to upper middle SE class population from South India. History of PNB was important and emerged as a strong risk factor for cervical cancer. Low parity was noted (median parity 2) among the cases since 90% of the study group had undergone tubal ligation. Hence, high parity as a risk factor in this

cohort does not apply. Long duration of sexual exposure, in fact, was one of the most important contributory factors to our reported prevalence of 1.36% in PAP smears tested in this age group. It is recommended that medical professionals, obstetric–gynecologic professionals, in particular, need to screen postmenopausal women as regularly as possible for cervical cancer irrespective of their SE status or parity. Special attention needs to be given to women reporting with PNB by making PAP smear testing mandatory.

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