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Research article

CARCINOMA CERVIX SCREENING – A CLINICOPATHOLOGICAL STUDY

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ABSTRACT

Background: Cervical carcinoma, the pathogenesis of which includes multiple factors was the leading cause of death 50 years ago and the mortality rate has been reduced to two thirds due to the effective screening by Pap smears which detected the cancers and precancerous conditions. **Objective:** The study was undertaken to analyze the routine cervical cancer screening on an age specific basis and to study the various predisposing factors of cervical carcinoma. **Methods:** We conducted an observation study on 1000 patients. The cervical smears collected were examined and predisposing factors were studied in these patients. **Results:** 1000 women above 20 years of age group were screened. There were 242 cases (24.2%) of dysplasia of which 133 cases (13.3%) were of mild dysplasia, 59 cases (5.9%) were of moderate dysplasia and 50 cases (5%) were of severe dysplasia. 29 cases (2.9%) showed invasive carcinoma. There were 564 (56.4%) inflammatory smears and 168 (16.8%) normal smears. Maximum number of dysplasia's and carcinomas were found in the age group above 40 years. These patients were from low income group, had no formal education, attained menarche at the age of 13-14 years, married at the age of 15-17 years, had three or more children and had marital life for more than 30years. **Conclusion:** Cervical cytology has been main stay of prevention and early diagnosis of cervical carcinomas. Due to its simplicity and low cost, pap smears can be used for mass screening. Cervical carcinoma has multiple etiological factors which play role in its pathogenesis.

Key words: Pap smear, Cervical carcinoma, Cytology

INTRODUCTION

Cervical carcinoma is the sixth most common visceral cancer in women and contributes to 5% of all cancer deaths in women worldwide. It accounts for approximately 15% of all cancers diagnosed in women world wide¹. In the developing world 1.7 million cases of carcinoma cervix and 5-13 million cases of precancerous lesions were recorded^{2,3}. The highest crude mortality rate is recorded in Southern Africa. In North America, Western Europe and Australia, the incidence of cervical cancer is low⁴. China has the least mortality rate¹. Death rate due to the cervical cancer has declined in the recent years

due to early detection of cancers and precancerous conditions. Cervical cancer screening by pap smears has reduced the morbidity due to cervical cancer by 53%. Susceptibility of cervical cancer for prevention by screening programme is determined by its high prevalence, a long detectable preclinical phase and benefit from early treatment. The Pap smear screening test if carried out properly is sufficiently sensitive and has high specificity, is of low cost and low risk to the patient⁵.

Mass cytological screening has shifted the presentation of cervical carcinoma from the clinical

to the preclinical stage. Though the incidence of cervical cancer has decreased significantly since 1960, age specific rates; however show an increase in young women, particularly those aged 25-29 years. It is not due to less effective screening of the younger population but the rise in incidence would be due to predisposition to risk factors⁶. In this study we tried to analyze the predisposing factors for carcinoma cervix and the age related incidence of cervical cancer in around Tirupathi.

MATERIAL AND METHODS

This cross sectional study includes 1000 patients who attended the gynecologic outpatient department in our hospital during the period of two years. Institutional ethical committee approved the study protocol. Informed consent was obtained from all the study participants. Pap smear from 1000 patients who were in the age group above 20 years was collected. The etiological and risk factors like age, parity, age at menarche, age at marriage, use of oral contraceptive pills, socio economic status and educational status of patients whose smears showed dysplastic changes were studied. The patients whose smears showed only inflammatory changes without dysplasia were excluded.

Smears were obtained from the patients with the help of Aylesbury spatula⁷. These smears were stained with Papanicolaou stain. Patient was placed in dorsal lithotomy or left lateral position. Non-lubricated (self-retaining) speculum was introduced into the introitus to visualize the cervix. Aylesbury spatula is placed in position and rotated in 360⁰ clock wise direction, so that sample from the ectocervix and endocervix including squamocolumnar junction are obtained. Specimen is spread evenly on glass slides. The smears collected were fixed in 95% of isopropyl alcohol for 15-30 minutes. These smears are stained with Papanicolaou stain. Smears of the patients which revealed dysplastic cells on microscopic examination were studied in detail. Patients which revealed dysplastic cells on microscopic examination were studied in detail.

OBSERVATION AND RESULTS

Cervical smears from 1000 women aged above 20 years who attended gynaecology out patient department were studied. A detailed history was recorded which included age, age of menarche, married life, number of pregnancies, age of last child, duration of menopause, use of oral contraceptive pills (OCP's), tobacco chewing or cigarette smoking, socio-economic status and educational status of women. The gynecological symptoms and clinical status of cervix was also studied. The women were grouped in 9 groups depending upon the age and various cytological features were studied (Table 1). There were 242 cases (24.2%) of dysplasias, of which 133 cases (13.3%) were of mild dysplasia, 59 cases (5.9%) were of moderate dysplasia and 50 cases (5%) were of severe dysplasia. 29 cases (2.9%) showed invasive carcinomas. There were 564 (56.4%) inflammatory smears and 168 (16.8%) normal smears (Table 1).

Highest incidences of mild and moderate dysplasia were seen in the age group of 40-50 years. Severe dysplasia and carcinomas were seen in the age group of 50-60 years. One case of invasive carcinoma was noted in the age group of 20 -30 years (Table 1). Maximum cases of invasive carcinoma, mild dysplasia, moderate dysplasia and severe dysplasia were noted in the menopausal age group when compared to reproductive age group (Table 2).

Epithelial changes in relation to age at menarche were studied and the highest incidence of dysplasia was noted in patients who attended menarche at the age of 13 years and invasive carcinoma in the patients who attained menarche at the age of 14 years (Table 3).

When the incidence of dysplasia in relation to the age at marriage was studied, it showed highest incidence of moderate, severe dysplasia and carcinoma in the patients who were married at the age of 15-17 years (Table 4). The incidence of carcinomas was found to be high in patients who had marital life of 31 years and above (Table 5). The study on parity of these patients showed that highest incidence of invasive carcinoma, moderate and severe dysplasias were noted in women who had three or more children. In nulliparous women only three cases were found to have mild dysplasia but there were no cases of moderate, severe dysplasia and invasive carcinoma (Table 6). Epithelial abnormalities in relation to economic status were also studied, which showed that incidence of dysplasia and invasive carcinomas was

maximum in the lower income group (Table 7) and these patients did not have formal education (Table 8).

Most of the patients with dysplasias presented with irregular vaginal bleeding and invasive carcinomas presented as post menopausal bleeding (Table 9). On clinical examination, mild and moderate dysplasia

cases presented as cervical erosion where as the cases with severe dysplasia and carcinoma presented as either growth on cervix or bleeding on touch (Table 10). Though the cigarette smoking, tobacco chewing and use of immunosuppressive drugs are considered as risk factors, in our study it did not reveal significant correlation (Table 11).

Table 1: Epithelial abnormalities in relation to age

Age in years	Total	Normal smears	Inflammatory smears	LSIL Mild dysplasia	HSIL Moderate severe dysplasia		Invasive carcinoma
20-30	203 (20.3%)	24 (2.4%)	150 (15%)	25 (2.5%)	2 (0.2%)	2 (0.2%)	-
31-40	304 (30.4%)	53 (5.3%)	187 (18.7%)	36 (3.6%)	14 (1.4%)	11 (1.1%)	3 (0.3%)
41-50	287 (28.7%)	51 (5.1%)	148 (14.8%)	44 (4.4%)	22 (2.2%)	13 (1.3%)	8 (0.8%)
51-60	128 (12.8%)	22 (2.2%)	56 (5.6%)	17 (1.7%)	11 (1.1%)	14 (1.4%)	9 (0.9%)
61 and above	78 (7.8%)	15 (1.5%)	23 (2.3%)	11 (1.1%)	10 (1%)	10 (1.0%)	9 (0.9%)

P<0.001.

Table 2: Epithelial abnormalities in menopausal and reproductive age group women

Age groups	Total	Normal smears	Inflammatory smears	LSIL mild dysplasia	HSIL Moderate Severe dysplasia		Invasive carcinoma
Menopausal	449 (44.9%)	90 (9%)	192 (19.2%)	73 (7.3%)	37(3.7%)	33 (3.3%)	24 (2.4%)
Reproductive	551 (55.1%)	75 (7.5%)	372 (37.2%)	60 (6%)	22(2.2%)	17 (1.7%)	5 (0.5%)

P<0.001

Table 3: Epithelial abnormalities in relation to age at menarche

Age at menarche in years	Total	Normal smears	Inflammatory smears	LSIL mild dysplasia	HSIL Moderate severe dysplasia		Invasive carcinoma
10-11 Years	40 (4%)	4 (0.4%)	24 (2.4%)	2 (0.2%)	5 (0.5%)	-	5 (0.5%)
12 years	276 (27.6%)	38 (3.8%)	153 (15.3%)	43 (4.3%)	17 (1.7%)	21 (2.1%)	4 (0.4%)
13 years	418 (41.8%)	69 (6.9%)	230 (23%)	64 (6.4%)	25 (2.5%)	23 (2.3%)	7 (0.7%)
14 years	185 (18.5%)	39 (3.9%)	114 (11.4%)	13 (1.3%)	7 (0.7%)	3 (0.3%)	9 (0.9%)
15 years and above	81 (8.1%)	15 (1.5%)	43 (4.3%)	11 (1.1%)	5 (0.5%)	3 (0.3%)	4 (0.4%)

P<0.005

Table 4: Epithelial abnormalities in relation to age at marriage

Age at marriage	Total	Normal smears	Inflammatory smears	LSIL Mild dysplasia	HSIL Moderate severe dysplasia		Invasive carcinoma
10-14 yrs	151 (15.1%)	31 (3.1%)	69 (6.9%)	21 (2.1%)	16 (1.6%)	8 (0.8%)	6 (0.6%)
15- 17 yrs	406 (40.6%)	50 (5.0%)	210 (21 %)	55 (5.5%)	33 (3.3%)	39 (3.9%)	19 (1.9%)
18yrs and above	443 (44.3%)	84 (8.4%)	285 (28.5%)	57 (5.7%)	10 (1 %)	3 (0.3%)	4 (0.4%)

P<0.001

Table 5: Epithelial abnormalities in relation to marital life

Married life	Total	Normal smears	Inflammatory smears	LSIL mild dysplasia	HSIL Moderate severe dysplasia		Invasive carcinoma
0-5 years	41 (4.1%)	7 (0.7%)	30 (3%)	4 (0.4%)	-	-	-
6-10 years	93 (9.3%)	18 (1.8%)	58 (5.8%)	15 (1.5%)	2 (0.2%)	-	-
11-20 years	267 (26.7%)	31 (3.1%)	187 (18.7%)	32 (3.2%)	5 (0.5%)	10 (1%)	2 (0.2%)
21-30 years	285 (28.5%)	48 (4.8%)	165 (16.5%)	37 (3.7%)	19 (1.9%)	13 (1.3%)	3 (0.3%)
31 years and above	314 (31.4%)	61 (6.1%)	124 (12.4%)	45 (4.5%)	33 (3.3%)	27 (2.7%)	24 (2.4%)

P<0.001

Table 6 Epithelial abnormalities in relation to parity

Parity	Total	Normal smears	Inflammatory smears	LSIL mild dysplasia	HSIL Moderate severe dysplasia		Invasive carcinoma
0	56 (5.6%)	22 (2.2%)	31 (3.1%)	3 (0.3%)	-	-	-
1	83 (8.3%)	17 (1.7%)	51 (5.1%)	11 (1.1%)	1 (0.1%)	3 (0.3%)	-
2	368 (36.8%)	53 (5.3%)	240 (24%)	53 (5.3%)	11 (1.1%)	8 (0.8%)	3 (0.3%)
3 and above	493 (49.3%)	73 (7.3%)	242 (24.2%)	66 (6.6%)	47 (4.7%)	39 (3.9%)	26 (2.6%)

P<0.001

Table 7: Epithelial abnormalities in relation to economic status

Economic status	Total	Normal smears	Inflammatory smears	LSIL mild dysplasia	HSIL Moderate severe dysplasia		Invasive carcinoma
Lower income group	701 (70.1%)	119 (11.9%)	374 (37.4%)	83 (8.3%)	50 (5%)	47 (4.7%)	28 (2.8%)
Middle income group	289 (28.9%)	42 (4.2%)	185 (18.5%)	49 (4.9%)	9 (0.9%)	3 (0.3%)	1 (0.1%)
Upper income group	10 (1%)	4 (0.4%)	5 (0.5%)	1 (0.1%)	-	-	-

P<0.001

Table 8: Epithelial abnormalities in relation to education status

Education status	Total	Normal smears	Inflammatory smears	LSIL mild dysplasia	HSIL Moderate severe dysplasia		Invasive carcinoma
No Formal education	665 (66.5%)	103 (10.3%)	345 (34.5%)	88 (8.8%)	52 (5.2%)	50 (5%)	27 (2.7%)
Primary education	279 (27.9%)	51 (5.1%)	180 (18%)	39 (3.9%)	7 (0.7%)	-	2 (0.2%)
Higher education	56 (5.6%)	11 (1.1%)	39 (3.9%)	6 (0.6%)	-	-	-

P<0.001

Table 9: Epithelial abnormalities and gynecological symptoms

Clinical symptoms	Total	Normal smears	Inflammatory smears	LSIL Mild dysplasia	HSIL Moderate severe dysplasia		Invasive carcinoma
Leucorrhoea	307 (30.7%)	16 (1.6%)	219 (21.9%)	56 (5.6%)	13(1.3%)	2 (0.2%)	1 (0.1%)
Dysuria	35 (3.5%)	8 (0.8%)	24 (2.4%)	3 (0.3%)	-	-	-
Irregular vaginal bleeding	192 (19.2%)	15 (1.5%)	90 (9%)	31 (3.1%)	25(2.5%)	24(2.4%)	7 (0.7%)
Post menopausal bleeding	71 (7.1%)	1 (0.1%)	13 (1.3%)	8 (0.8%)	8 (0.8%)	22(2.2%)	19 (1.9%)
Pain in Lower abdomen	194 (19.4%)	41 (4.1%)	121 (12.1%)	23 (2.3%)	8(0.8%)	1 (0.1%)	-
Mass per vagina	78 (7.8%)	25 (2.5%)	39 (3.9%)	7 (0.7%)	5(0.5%)	-	2 (0.2%)
Routine check up	123 (12.3%)	59 (5.9%)	58(5.8%)	5 (0.5%)	-	1 (0.1%)	-

P<0.001

Table 10: Epithelial abnormalities in relation to clinical lesions

Clinical lesions	Total	Normal smears	Inflammatory smears	LSIL mild dysplasia	HSIL Moderate severe dysplasia		Invasive carcinoma
Erosion cervix	230 (23%)	6 (0.6%)	137 (13.7%)	55 (5.5%)	19 (1.9%)	13 (1.3%)	-
Hypertrophied cervix	63 (6.3%)	10 (1%)	34 (3.4%)	12 (1.2%)	5 (0.5%)	1 (0.1%)	1 (0.1%)
Suspicious cervix (growth/ bleeding on touch)	82 (8.2%)	-	3(0.3%)	10(1%)	10 (1%)	32 (3.2%)	27 (2.7%)
Senile vaginitis	41 (4.1%)	9 (0.9%)	22 (2.2%)	4 (0.4%)	4 (0.4%)	2 (0.2%)	-
Polyp	4 (0.4%)	1 (0.1%)	2 (0.2%)	1 (0.1%)	-	-	-
Endocervicitis	155 (15.5%)	5 (0.5%)	123 (12.3%)	18 (1.8%)	8 (0.8%)	1 (0.1%)	-
Prolapsed	87(8.7%)	29(2.9%)	40 (4%)	12(1.2%)	5(.5%)	-	1 (0.1%)
Normal	338 (33.8%)	105(10.5%)	203 (20.3%)	21 (2.1%)	8 (0.8%)	1 (0.1%)	-

Table 11: Epithelial abnormalities in relation to risk factors

Risk factors	Total	Normal smears	Inflammatory smears	LSIL mild dysplasia	HSIL Moderate severe dysplasia		Invasive carcinoma
Cigarette smoking	-	-	-	-	-	-	-
Tobacco chewing	105(10.5%)	16 (1.6%)	41 (4.1%)	18 (1.8%)	12 (1.2%)	10 (1%)	8 (0.8%)
Immunosuppressive drugs	1 (0.1%)	1 (0.1%)	-	-	-	-	-

DISCUSSION

The etiology of cervical neoplasia, which is considered to be the third most common cancer in women, has been studied epidemiologically for over 150 years⁸. Epidemiologically cervical cancer behaves like a sexually transmitted disease and is more common in women who have multiple sexual partners⁹, or whose partners are promiscuous¹⁰ and is absent in virgins. Epidemiological data has shown

that cervical carcinoma is caused by sexually transmitted agent, Human Papilloma virus (HPV) which plays an important role in oncogenesis. Though HPV is considered to be an important etiological factor, the presence of other risk factors along with HPV infection are important in deciding the outcome of the disease i.e. whether HPV infection will regress or progress to cervical cancers¹¹.

The U.S. Preventive Services Task Force (USPSTF) has recommended that women aged 21 to 65 years should undergo cytological screening for every 3 years. If the women (30 to 65 years) want to lengthen the interval for Pap smear screening, then the combination of Pap smear test and HPV testing for every 5 years is recommended. The USPSTF does not recommend the cervical cancer screening in women younger than 21 years, for women elder than 65 years whose previous cytology smears were normal, women who had undergone hysterectomy with removal of the cervix without any previous precancerous lesion or cancers and testing for HPV alone or along with cytology in women who are younger than 30 years¹².

Most of the patients who attended the Government Maternity Hospital, Tirupathi were of low socio economic group. Low, moderate and high income groups differ in various aspects like nutritional and vitamin deficiencies, parity, married life, age at marriage. Hence socioeconomic group is the index of all the above factors which share their contribution in the genesis of cancer cervix.

The incidence of invasive cancer in our study was 2.9% which coincided with the results of JS Misra (2001)¹³. In our study, severe dysplasia and invasive carcinomas were common after 50 years because of altered hormonal balance that are usually seen in the female genital tract. The role of hormonal factors in the etiology of cervical cancer had been underscored by recent studies which identified several independent risk factors like multiple births, early age at marriage and marital life.

In our study, highest incidence of invasive carcinomas and dysplasias were found in women who had more than 30 years of married life. This shows that there is intimate relationship between married life and incidence of cancer cervix. Parazzini et al (1989) suggested that with every pregnancy, women would have double the risk compared to women without children and the risk was ten times more than unmarried women¹⁴. Other studies have shown that the incidence was high in women who marry early and tend to conceive more number of times as they are exposed to longer duration in sexual activity.

The cigarette smoking /tobacco chewing was attributed as one of the risk factors of cervical neoplasia. In our study out of 29 cases of invasive carcinoma, cases were found to be associated with

tobacco chewing and also few cases of dysplasias had association with tobacco chewing. Cigarette smoking has been associated with increased risk of cervical cancer, especially among long term or high intensity smokers¹⁵. Smoking constituents have been found in cervical mucous, but the biologic mechanisms underlying the smoking-cervical cancer relationship have not been identified.

The use of oral contraceptive pills (OCPs) is also another risk factor. But because most of the patients attending outpatient department are low socio-economic group without formal education, the number of patients, using OCP's were very few. After elaborate study it is clearly evident that no single factor can be named as the cause of cancer cervix. Many factors may play part and contribute to the causation of cancer like prolonged sexual life, multiple sexual partners, parity, low socio-economic status, the virus infections and genetics.

Immunosuppression has been found to be associated with dysplastic changes in the cervix. HPV DNA is detected more often in pregnant women who have transient depression of cell mediated immunity. More recently, an increased risk of cervical neoplasia has been noted in patients infected with HIV¹⁶. Immunosuppression is considered to inhibit clearance of papilloma virus and promote their reactivation¹⁷.

Most of the frank invasive carcinomas presented as growth on cervix or cervix which bleeds on touch which has also been found to be the same in study by JS Misra. Many cases of dysplasias presented as erosion cervix. Other symptoms are leucorrhoea, dysuria, irregular vaginal bleeding, pain in lower abdomen and mass per vagina.

For the prevention of cervical carcinoma and precursor lesions American Cancer Society (ACS) recommends Human Papilloma virus vaccines for females aged 11 to 12 years. It also suggests that females as young as 9 years may receive HPV. For the females aged 13 to 18 years, HPV vaccination should be given to catch up missed vaccination or complete the vaccination series. Vaccination is not recommended for women over age of 26 years because ideally the vaccination should be done prior to genital HPV exposure as the benefit is likely to diminish with increasing number of lifetime sexual partners. Even after the vaccination, screening for the cervical intraepithelial neoplasia and cancer should continue. Two prophylactic HPV vaccine are

available i.e. Gardasil which protects against HPV types 6, 11, 16 and 18 (quadrivalent) and Cervarix which protects against types 16 and 18 (bivalent) ¹⁸.

CONCLUSION

Cervical carcinoma is caused not due to single etiological factor but multiple independent risk factors like age, age at menarche, age at marriage, parity, educational and economic status, use of oral contraceptives, cigarette smoking play role in the pathogenesis. Due to simplicity, low cost and validity of the Pap smear screening, it becomes apparent that this test could be effectively used to detect early cancer and premalignant changes in cervix uteri.

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