RESEARCH ARTICLE

Opportunistic Screening for Cervical Cancer in a Tertiary Hospital in Karnataka, India

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Abstract

The incidence and mortality of cervical cancer remains high in India even after sixty years of introduction of the Pap smear (cervical cytology) which is an effective means of identifying preinvasive lesions of carcinoma cervix. The morbidity and mortality due to cervical cancer has come down drastically in countries with well established screening programmes at national level. This study aims at screening women for cervical cancer opportunistically during their visit to hospital and to study various types of neoplastic and non-neoplastic lesions of the cervix by cervical smear study (Pap smear study). In the present study, a total of 350 cervical smears were studied. The age of patients ranged from 19 years to 80 years with mean age being 37.5 years. Out of 350 cases, the diagnosis of neoplasia was given in 43 cases and 258 cases were diagnosed as inflammatory smears. Forty-cases were normal and 9 cases were inadequate to evaluate. Forty-three patients who were found to have neoplastic lesions on cytology were referred for further investigations like colposcopy and biopsy to confirm the diagnosis and avail proper treatment. Limitation of the present study was small sample size as all female patients aged between 20 and 60 years visiting hospital were not included in the screening, other screening tests like VIA (visual inspection with acetic acid test) and HPV DNA (human papilloma virus) tests were not done. Until the time centrally organised screening programmes for cervical cancer are established in India, arrangements should be made for hospital based opportunistic screening for all women attending hospital. The cost effectiveness of different screening tests for cervical cancer should be evaluated.

Keywords: Cervical cancer - Pap smear - opportunistic screening

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Introduction

The incidence and mortality of cervical cancer remains high in India even after sixty years of introduction of Pap smear (cervical cytology) which is an effective means of identifying preinvasive lesions of carcinoma cervix. This can be attributed to multiple factors like lack of well organised screening programme which in turn is dependent on health system and available resources, ignorance of people regarding the disease and time constraints of the doctors. The morbidity and mortality due to cervical cancer has come down drastically in countries with well established screening programmes at national level (www.cytoindia.com/cytology%20eqa/ccsp%20guidelines.pdf) (Roderick et al., 2006). With an increase in the incidence of HIV infection there is an increase in the incidence of HPV infection of cervix. HPV infection is a known precursor of preneoplastic and neoplastic lesions of the cervix (Sankaranarayanan et al., 2009).

However, in India till date there are no suitable, large scale, cost effective; population based screening programs to detect prevalence of HPV infection and preinvasive stages of carcinoma cervix. Hence, there is a need to introduce hospital or institution based screening programs which may not be as effective as nationionally organised screening programmes, but will definitely help to reduce the burden to some extent. This study aims at screening women for cervical cancer opportunistically during their visit to hospital and to study various types of neoplastic and non-neoplastic lesions of the cervix by cervical smear study (Pap smear study).

Materials and Methods

During the two year study period 350 Pap smears (cervical smears) were obtained from female patients visiting JSS Hospital, Mysore, Karnataka, India. Cervical smear was taken after obtaining consent of the patient. Cervix of the patient was exposed adequately with a speculum. The squamocolumnar junction was visualized, with the hooked end of Ayre's spatula, squamocolumnar junction was scraped gently throughout its circumference

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and material was transferred to glass slides. Two such smears were fixed with 95% alcohol immediately and stained by Papanicolaou stain. Slides were reported by Pathologists and cases with abnormal findings were suggested for follow up or biopsy/colposcopic examination.

Results

In the present study, a total of 350 cervical smears were studied. The age of patients ranged from 19 years to 80 years with mean age being 37.5 years. The major presenting complaint was white discharge per vaginum followed by intermenstrual irregular bleeding, and postmenopausal bleeding.

Out of 350 cases, the diagnosis of neoplasia was given in 43 cases and 258 cases were diagnosed as inflammatory smears. Fourty-cases were normal and 9 cases were inadequate to evaluate. Table 1 shows age wise distribution of cytologic diagnosis and percentage of neoplastic and non-neoplastic lesions is given in Table 2.

The percentage of malignant lesion was 4.65% and of premalignant lesion was 95.35%. Ratio of premalignant to malignant lesions was 20.5:1. In the premalignant lesions, HSIL constituted to 34.89% and LSIL to 60.46%. Maximum number (30.76%) of LSIL were seen in second decade (21-30 years) whereas HSIL (53.33%) were seen in fifth decade (51-60) and carcinoma in fifth and fourth decade (41-50).

Table 1. Agewise Distribution of Cytologic Lesions on Pap Smears

Age in years	Non Neoplastic Lesions		Neoplastic Lesions	
	No of cases	%	No of cases	%
11-20	5	1.64	0	0
21-30	116	37.8	9	20.9
31-40	95	30.9	7	16.2
41-50	63	20.5	10	23.2
51-60	17	5.54	15	34.8
61-70	8	2.64	1	2.32
71-80	3	0.98	1	2.32

Cytology

Squamous cell carcinoma (Figure 1a): Two cases were diagnosed as squamous cell carcinoma which showed malignant squamous cells in aggregates and in singles. The cells had abundant to moderate amount of cytoplasm with large round to oval hyperchromatic irregular nuclei. Background showed inflammatory cells, necrotic debris and mild haemorrhage.

High Grade Squamous Intraepithelial Lesion (HSIL) (Figure 1b). Fifteen cases showed dysplastic cells with marked increase in nuclear cytoplasmic ratio. Cells had moderate to scanty amount of cytoplasm with hyperchromatic pleomorphic nucleus. Chromatin was coarse and irregularly clumped with inconspicuous nucleoli. Also seen were many normal superficial and intermediate squamous cells. Background showed a few inflammatory cells. All these cases were given a diagnosis of HSIL.

Low Grade Squamous Intraepithelial Lesion (LSIL) (Figure 1c): Twenty six cases were grouped into this category. All cases showed cellular smears with few

Table 2. Distribution of Neoplastic and Non-neoplastic Lesions on Cytology

			No. of cases	%
Neoplastic Lesions	1	Malignant	2	4.65
	2	Premalignant	41	95.35
	2a	a) HSIL	15	34.89
	2b	b) LSIL	26	60.46
		Total	43	100
Non neoplastic Lesions	1	Reactive cellular changes	252	97.67
	1a	Nonspecific inflammation	154	59.68
	1b	Squamous metaplasia	90	34.88
	1c	Reactive endocervical cells	3	1.16
	1d	Atrophic vaginitis	5	1.94
	2	Specific Infections	6	2.33
	2a	Trichomonas	5	1.94
	2b	Candida	1	0.39
		Total	258	100

*HSIL: High Grade Squamous Intraepithelial Lesion; LSIL: Low Grade Squamous Intraepithelial Lesion

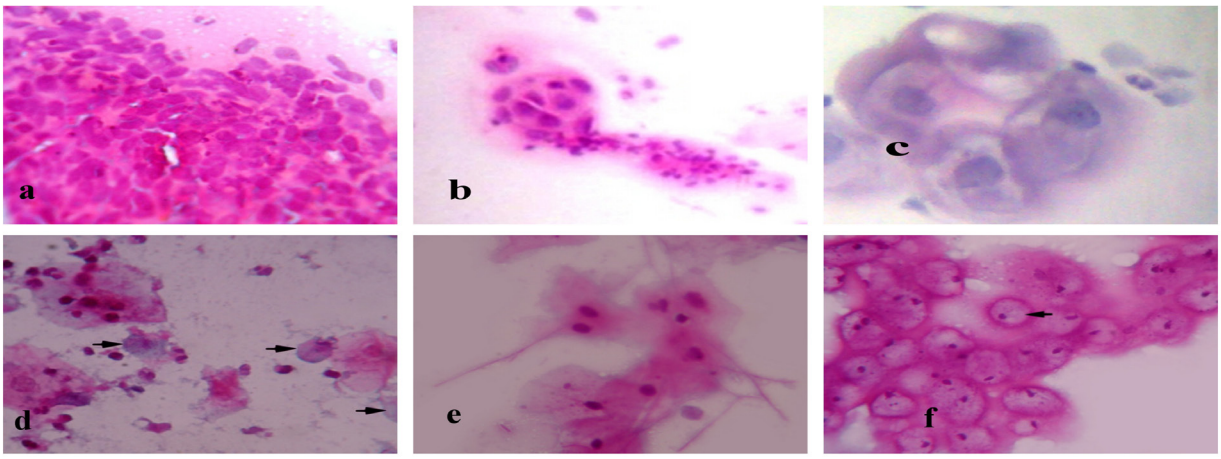

Figure 1. a) Squamous Cell Carcinoma, showing malignant cells displaying pleomorphic and overcrowded nuclei (Pap, 10×40); **b) HSIL – Cluster of Cells,** showing increased N/C ratio with hyperchromatic nuclei and coarse chromatin (Pap, 10×40); **c) LSIL – Group of Intermediate Squamous Cells,** showing perinuclear halo around large hyperchromatic nuclei (Koilocytic change) (Pap, 10×40); **d) Smear,** showing pear shaped Trichomonas vaginalis organisms (arrows) in an inflammatory background (Pap, 10×40); **e) Smear,** showing pseudohyphae of Candida in candidiasis (Pap, 10×40); and **f) Superficial Squamous Cells,** showing perinuclear halo (arrow) in Candidiasis (Pap, 10×40)

Table 3. Ratio of Non Neoplastic and Neoplastic Lesions

Study	Non neoplastic	Neoplastic	Ratio
Van der Graaf et al. (1987)	162626	2559	63.5:1
Murthy et al. (1990)	84889	2125	39.9:1
Mostafa et al. (2000)	112091	815	137.5:1
Bhatia et al. (2001)	100	16	6.25:1
Robyr et al. (2002)	740	27	27.4:1
Present study	258	43	6:1

Table 4. Comparison of Distribution of Neoplastic Lesion

Study	LSIL	HSIL	Carcinoma	Total
Lozowski et al. (1982)	36 (28.30%)	89 (70.10%)	2 (1.57%)	127
Klinkhaemer et al. (1988)	8 (6.66%)	108 (90.00%)	4 (3.33%)	120
Kashyap et al. (1995)	1253 (59.02%)	657 (30.90%)	213 (10.10%)	2123
Mostafa et al. (2000)	162 (22.91%)	378 (53.46%)	167 (23.62%)	707
Present study	26 (60.46%)	15 (34.88%)	2 (4.65%)	43

*HSIL: High Grade Squamous Intraepithelial Lesion, LSIL: Low Grade Squamous Intraepithelial Lesion

clusters of atypical cells showing mild increase in nuclear cytoplasmic ratio. Nucleus was slightly enlarged with fine granular chromatin. Few cells had hyperchromatic and irregular nuclei with perinuclear halo (koilocytic change). Background showed acute inflammatory cells.

Non neoplastic Lesions (Figure 1d-f). Cases in this category predominantly showed superficial and intermediate cells in sheets and singles with few showing squamous metaplastic cells, reactive endocervical cells, and parabasal cells. Almost all cases showed dense to moderate amount of neutrophils. Six cases showed Trichomonas vaginalis organisms and one case showed candidiasis.

Discussion

In India, till date there are no well organized comprehensive population based screening programme for cervical cancer, this could be because cervical carcinoma is not included in the top ten health priorities list (Basu et al., 2009) or the policy makers are not aware of the problem, or partly due to lack of resources. As a result asymptomatic women are not screened for cervical cancer, even once in their life time (Giftson et al., 2011).

However, many efforts are being carried out to formulate a uniform health strategy in low resource countries like, India by WHO through IARC and ACCP (International Agency for Research in Cancer, Alliance for Cervical Cancer Prevention), and Government of India through ICMR and NCCP.

The National Cancer Control Programme (NCCP) was started in 1975-76 by government of India. Under NCCP, 1 lakh Pap Smear kits for early detection of cancer cervix in women were supplied to 12 Regional cancer centres (RCC) in 1998-1999, Training of trainers programme regarding awareness, prevention, early detection and treatment in Breast and cervical cancers in women was held at Tata Memorial Hospital (TMH) Mumbai and CNCI (RCC) Kolkatta in 1999 and orientation training workshops for cytopathologists regarding quality assurance of Pap smear test were carried out at five RCCs (Gupta et al., 2002).

In November 2005 (In collaboration with NCCP and WHO) the department of Cytology and gynaecological Pathology at the postgraduate institute of Chandigarh organized meeting of the experts and proposed NCCP guidelines for cervical cancer screening programme to be implemented in areas which do not have the capacity for undertaking Pap smear based cervical screening programmes for large populations. For reasons not known, until today this has not been implemented in any of the district or state in India (NCCP guidelines for cervical screening, 2006; www.cytoindia.com/cytology%20eqa/ccsp%20guidelines.pdf).

The Indian Medical council introduced National Cancer Registry Programme (NCRP) in December 1981. Initially the programme began with setting three population based cancer registries (PBCRs) at Bangalore, Chennai and Mumbai and three hospital based cancer registries (HBCRs) at Chandigarh, Dibrugarh and Thiruvananthapuram. And now there are fourteen PBCRs under NCRP network. The main functions of these PBCRs is to provide reliable data on the magnitude and patterns of cancer that help in undertaking epidemiological studies, and designing, planning, monitoring and evaluation of cancer control activities under the National Cancer Control Programme (NCCP).The NCRP is a long term activity of the ICMR. The office is located in Bangalore. It is assisted by a steering committee and a Monitoring committee that meets periodically to oversee and guide its functioning. The periodic publication of NCRP will help in assessing the effectiveness of screening programme (NCRP, 2003; www.icmr.nic.in/ncrp/first_report_2003-04).

WHO in coordination with IARC and ACCP is also helping the low resource countries to fight against cervical cancer. During 1999 to 2003 with the support of Bill and Melinda gates foundation the IARC/WHO have started several studies in the following states of India: Dindigal district, Tamil Nadu, Barshi, Maharastra, Calcutta, Coimbatore, Hyderabad, Jaipur, kannur, Mumbai, New Delhi, Trivandrum and CMC Vellore. These studies included non randomised controlled trials, randomised trials, cross sectional studies and demonstration projects on cervical cancer screening. The objectives of these studies were to know the accuracy of different screening tests available for cervical cancer, cost effectiveness of each test, cure rates of CIN, side effects and complications of treatment of CIN, and determinants of participation (Sankaranarayanan, WHO/IARC; www.screening.iarc.fr). Conclusions of these studies were as follows: Cytology as a single test had better sensitivity, specificity and predictive value and in low resource country which cannot afford for cytology based screening tests, visual screening tests are promising methods for the early detection of cervical cancer (Shastri et al., 2005).

The major drawback of visual tests is its lower specificity which means large number of women may receive unnecessary treatment or additional investigations. Developing countries can implement good quality cytology even in rural setting with reasonable investment (Sankaranarayanan et al., 2005).

The sensitivity of HPV ranged from 45.7-80.75% and its specificity was significantly higher than that of visual

tests, but lower than that of cytology. Due to high cost and requirement of sophisticated laboratory HPV test cannot be used in low resource countries (Sankaranarayanan et al., 2004). Apart from these sanctioned projects in selected districts, Government of India is not intending to introduce population based screening in almost the entire country.

Recently Government of India initiated an integrated National Programme for Prevention and Control of Cancers, Diabetes, Cardiovascular Diseases and Stroke (NPCDCS) in 100 districts of 21 states in 2011. National Cancer Control Programme has been integrated under NPCDCS. It is painful that cervical cancer screening and prevention is neglected against other bigger problems like diabetes and stroke in this ongoing programme (NPCDCS Guidelines).

Hence we think India having many private Medical Colleges and hospitals rendering services to rural people, should strengthen opportunistic screening (independent of national policies) and help the country to reduce burden of cervical cancer.

It is needless to say the importance of preventing a cancer than treating it. The best way of treating a cancer is to prevent its occurrence. All medical practitioners are well aware of this. There are many cancers which can be diagnosed at early asymptomatic stage by applying simple screening tests. Cervical cancer being one among those is an ideal disease for screening. Screening can be achieved through two ways: 1.Nationally or regionally organised screening programmes, which aims at covering >80% of the population at risk or 2. Opportunistic screening programs which are independent of nationally organised screening programs are focussed on women who are visiting health services for other reasons (Adab et al., 2004; Miles et al., 2004).

The cytologic diagnosis of cervical smears has become a very important screening test for the detection of preinvasive and invasive cervical epithelial abnormalities. Three hundred and fifty cases including neoplastic and non neoplastic lesions were studied in the present study. An attempt has been made to compare the various parameters in the study with the results obtained by different workers.

The mean age in the present study was 35.7 years which was comparable to the study of Chang et al. (1996) in which the mean age was 37 years. The mean age was slightly higher in other studies as reported by Autier et al. (1996) Mostafa et al. (2000) and Robyr et al. (2002).

The above Table 3 shows wide variation in the ratio of non neoplastic to neoplastic lesions in different studies, indicating the geographical influence on occurrence of cervical carcinoma. The results in the present study were similar to that reported by Bhatia et al. (2001). However, others (Table 4) found increase in the ratio.

In the present study, the ratio of premalignant to malignant lesions was 20.5:1, which was comparable to study of Klinkhaemer et al. (1988) where the ratio was 29:1. However, the rate of premalignant lesions was much higher as reported by Lozowski et al. (1982) with ratio of 62.5:1. Mostafa et al. (2000) had found a lower rate of premalignant lesions, the ratio being 3.2:1.

Premalignant lesions were higher in the studies conducted by Lozowski et al. (1982) and Klinkhaemer et al. (1988) indicating that malignant lesions were less common in developed countries. Early detection of premalignant lesions in developed countries prevents the progress of premalignant lesions to malignant lesions.

The percentage of LSIL and HSIL was 60.46% and 34.88% respectively in the present study and similar findings were reported by Kashyap et al. (1995) where LSIL was 59.02% and HSIL was 30.94%. However, others (Table 4) have reported a higher percentage of HSIL compared to LSIL. This probably indicates variation in individual interpretation of SIL. As with the other studies, the percentage of carcinoma was lower than the percentage of dysplasia in the present study.

Mean age for preinvasive lesions was 45.8 yrs in the present study. Bhatia et al. (2001) found mean age of 44 years in their study for preinvasive lesions, indicating increased incidence of preinvasive lesiosn in elderly females.

Average age of carcinoma cervix in the present study was found to be 51 years which was similar to that reported by Bhatia et al. (2001) where it was 49.5 years.

Bhatia et al. (2001) in their study, found maximum cases of dysplasia in the age group of 31-40 years and carcinoma in the age group of 51-60 years, whereas in the present study, maximum cases of dysplasia were detected in 51-60 years age group and carcinoma in 41-60 years age group. The difference in the age could be due to wide variation in selection criteria. They also observed that 80% of cases of carcinoma cervix were from poor socio-economic status and from rural population. Similar findings were noted in the present study also.

Specific infections accounted for a very small percentage (2.33%) of cases in the present study as compared to the study of Malik et al. (2001). The percentage of specific infections was 8% in their study and was mainly due to Coccobacilli causing shift in vaginal flora. The common infective organism found in the present study was Trichomonas (1.94%) followed by Candida (0.39%). Robyr et al. (2002) noted a high incidence of Gardnerella vaginalis. The majority of inflammatory cases were due to nonspecific inflammation in the present study. Similar findings were reported by Malik et al. (2001).

The major presenting complaint was white discharge per vagina in the study of Bhatia et al. (2001) (26.8%). In the present study, majority of the patients complained of white discharge per vagina (35.14%), the other symptoms being post menopausal bleeding in 24.28% and irregular bleeding in 25.14%. Bhatia et al. (2001) and Sunanda et al. (1968) reported vaginal discharge and pain lower abdomen as common complaints in women with dysplasia. In the present study also, vaginal discharge was the common complaint in women with dysplasia. Chief complaints in carcinoma cervix was contact bleeding as reported by Bhatia et al. (2001). In the present study, one case presented with post menopausal bleeding and the other presented with irregular menstrual cycles.

In conclusion 43 patients were found to have neoplastic lesions on cytology in the present study and all of them were referred for further investigations like colposcopy and biopsy to confirm the diagnosis and avail proper treatment. In India with lack of centrally

organised population based screening program for cervical cancer, we hope such opportunistic screening with little extra effort to cover more number of women at risk by counselling and encouraging them to involve in screening program regularly may help to reduce the country's burden of cervical cancer. However, opportunistic screening may not be as efficient as organised programme due to low coverage of target population. Hence for a country like India with great burden of carcinoma cervix population based centrally organised screening program is imperative to reduce the mortality and morbidity of cervical cancer.

Limitation of the present study was small sample size as all female patients aged between 20 and 60 years visiting hospital were not included in the screening, other screening tests like VIA (visual inspection with acetic acid test) and HPV DNA (Human Papilloma Virus) tests were not done.

Until the time centrally organised screening programmes for cervical cancer are established in India, arrangements should be made for hospital based opportunistic screening for all women attending hospital. The cost effectiveness of different screening tests for cervical cancer should be evaluated.

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