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Original Article

Clinicopathological Presentation of Cervical Cancer in Bhopal

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Abstract

Aim: To study the clinicopathological spectrum of cervical cancers in tertiary care center to assess scenario in Central India. **Materials and Methods:** Retrospective study in the Department of Pathology in our institution to evaluate cases of cervical cancers from January 2014 to August 2015. Histopathological diagnosis was correlated with age, symptoms, gravida, Federation of Gynecology and Obstetrics staging, and other relevant clinical details wherever deemed necessary. The biostatical analysis was performed for quantitative data student's *t*-test was applied. *P* value was considered statistically significant if $P < 0.05$. **Results:** A total of 180 cases were of neoplasia cervix. Majority of cases were squamous cell carcinoma type, i.e., 96.6% (174 cases) followed by adenocarcinoma constituting only 2.8% (5 cases) with a mean age of 50.7 years and average gravida of 3.78. Majority of cases (50.01%) complained of postmenopausal bleeding followed by abnormal spotting (26.67%) and lower abdominal pain (7.78%). The most common presentation was in Stage IIB with 45.56% (82) cases. **Conclusion:** Histomorphology remains the mainstay of diagnosis of cervical cancers. In low compliance settings such as ours, colposcopy-guided biopsy is the preferred course of management, especially in elderly females to be definite to rule out or diagnose neoplasia. National level cervical cancer program is immediate need of the hour and should include human papilloma virus vaccine, awareness, and screening programs as well as treatment assistance for low socioeconomic strata.

Keywords: *Cancer, Central India, cervix, clinicopathological*

Introduction

Cancer of the cervix is a global health problem, especially in developing countries like India where effective screening programs are lacking in planning, organization, and implementation levels.

It is also the fourth most common cause of cancer death (266,000 deaths in 2012) in women worldwide accounting for 7.5% of all female cancer deaths. Almost nine out of 10 (87%) of cervical cancer deaths occur in less developed countries, and more than one-fifth of all new cases are diagnosed in India.[1] Organized population-based screening linked to treatment of the detected neoplasia can lead to more than 70% reduction of disease-related mortality.[2] The mortality and morbidity burden poses a heavy economic burden on families.[3] Mortality due to cervical cancer is also an indicator of health inequities,[4] as 87% of all deaths due to cervical cancer are in developing, low- and middle-income countries.[5]

Cervical cancer prevention programs include a 3-stage intervention: Screening by Pap tests/cervical cytology, colposcopic evaluation of screen positives, and directed biopsy of abnormal looking cervical tissue for diagnosis and excisional or ablative treatment of cervical tissue in women diagnosed with precancerous/cancerous lesions. The incidence of cervical cancer can be decreased by regular screening and treatment of precancerous lesions. Although Pap smear is central to screening, it has some limitations, most important being its limited sensitivity which is between 47% and 62% and the subjective interpretation of the results.[6] Survival rates for cervical cancer can be further improved by establishing effective cancer treatment programs. Cervical cancer is preceded by a long period of premalignant disease with increasing morphological atypia and the potential for progression to malignancy. On an average, cervical cancer takes at least a decade to develop.

The pattern of gynecological malignancies varies among nations and even within health institution in the same country.

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Understanding the histopathological pattern of these will help in the management of the patient. Therefore, the histopathological examination of the biopsies of cervical lesions is the single best gold standard for the diagnosis of the lesions of the cervix.[7] The aim of the following study is to study cases of cervical cancers. Ours being a tertiary care center with high patient load can give a better picture of the current scenario to give histomorphological spectrum and establish the clinicopathological correlation of cervical cancers in Central India. On the basis of this, a detailed histomorphological study of the neoplastic lesions of the cervix was taken up our institution.

Materials and Methods

All the uterine cervical biopsies and hysterectomy specimens (for cervical lesions) received in our institution were evaluated retrospectively from January 2014 to August 2015. After standard grossing and processing procedure, the tissues were examined in hematoxyline and eosin stained slides and histopathological evaluation was done. The findings were correlated with age, symptoms, gravida, parity and other relevant clinical details wherever deemed necessary. The biostatical analysis was performed using program IBM SPSS (Statistical Package for the Social Sciences), for quantitative data student's *t*-test was applied. P value was considered statistically significant if $P < 0.05$, and highly statistically significant if $P < 0.01$.

Results

A total of 180 cases were of neoplasia cervix. Among all the neoplastic lesions, moderately differentiated squamous cell carcinoma with 92 (51.11%) cases was the most common histological type of carcinoma encountered in our study followed by Nonkeratinizing Squamous Cell Carcinoma (NKSCC), Well-Differentiated Squamous Cell Carcinoma (WDSCC), Poorly Differentiated Squamous Cell Carcinoma(PDSCC), Adenocarcinoma (AdenoCa), and Adenosquamous carcinoma with 25.56% (46), 11.67% (21), 8.33% (15), 2.78% (5), and 0.56% (1) cases, respectively.

Thus, the majority of cases were of squamous cell carcinoma type, i.e., 96.6% (174 cases) followed by AdenoCa constituting only 2.8% (5 cases). Among 174 squamous cell carcinoma cases, 128 (73.5%) cases were keratinizing and 46 (26.4%) cases constituted nonkeratinizing type.

Regarding age distribution, the mean age for neoplastic lesion was 50.67 years with a high standard deviation of 10.86. Age distribution according to histomorphological diagnosis is shown in Table 1.

Youngest patient was of 26 years age and oldest was 70 years. Mean age was not significantly different for different histological subtypes of squamous cell carcinoma with majority being postmenopausal. The youngest female case of carcinoma was nulligravida and had received no vaccination for human papilloma virus (HPV), however, sexual history was unreliable.

Table 1: Age distribution for neoplastic lesion of cervix

Diagnosis	Total cases	Mean age	Minimum age	Maximum age
MDSCC	92	50.6	30	75
NKSCC	46	51.0	30	70
WDSCC	21	50.4	26	66
PDSCC	15	52.1	30	70
Adenoca	5	45.8	40	60
Adenosquamous	1	45.0	45	45

MDSCC – Moderately differentiated squamous cell carcinoma;
NKSCC – nonkeratinizing squamous cell carcinoma;
WDSCC – Well-differentiated squamous cell carcinoma;
PDSCC – Poorly differentiated squamous cell carcinoma

Clinical presentation of cervical lesions

The clinical presentation of women was varied. Majority of cases (50.01%) complained of postmenopausal bleeding followed by abnormal spotting (26.67%) and lower abdominal pain (7.78%).White discharge with abdominal pain constituted a mere 6.66% of cases followed by growth (6.11%), postcoital bleeding (1.67%), and pyometra (1.11%).

Gravida

Average gravida of females in our study was found to be 3.78. Twenty-six (14.4%) cases had 0–2, 113 (62.7%) had 3–4, whereas 42 (23.3%) cases were grand multipara (>5).

Staging of cervical cancers

According to the Federation of Gynecology and Obstetrics (FIGO) staging of patients included in our study, most common presentation was in Stage IIB with 45.56% (82) cases followed by Stage IIIB with 21.02% (37) cases and IIIB with 21.02% (29) cases. As per the WHO, advanced cervical cancer means cancer that has grown into tissues around the cervix, i.e., Stage IIB, or spread further. In the present study, 158 (87.8%) women presented in advanced stage of cervical cancer. Cases amenable to early treatment and better prognosis constituted only a handful (Stage IB), i.e., a mere 3.33%. While cases presenting with distant metastasis and worst prognosis (Stage IV) were mainly in older age group.

On the basis of FIGO staging with respect to different histological subtypes, 92.9% of cases of keratinizing squamous cell carcinoma were in advanced stage compared to 73.9% in nonkeratinizing squamous cell carcinoma. All cases of adenocarcinoma presented in advanced stage.On statistical analysis, keratinizing squamous cell carcinoma were found to have poor prognosis compared to nonkeratinizing squamous cell carcinoma and the difference was highly significant with $P = 0.006$ ($P < 0.01$). However, with respect to AdenoCa, results were insignificant.

Other factors

Majority of females had poor personnel hygiene habits. Only 4% used oral contraceptives, a minority used barrier method while majority used no contraceptives and had tubal sterilization after family completion.

None of the females had received any HPV vaccines in their lifetime. There was a nominal level of awareness with regard to this vaccination and those few who were willing perceived the cost to be high as per their financial affordability.

Majority of women in our study had menarche at 12–13 years of age and had first sexual exposure before the age of 20 years. A majority of them also had their first conception before reaching 20 years and almost all had completed their family by 30 years of age. Breast feeding was nonexclusive.

Discussion

Cancers of cervix have a considerable burden on our health system as well as has social and financial implications. We studied the histomorphological variations of cancer cervix in our institute. Squamous cell carcinoma was the most common histological type of cervical cancer as observed by Olu-Eddo *et al*.,[8] Okoye,[9] Abudu *et al*.,[10] Pathak *et al*.[11] and Ikechebelu *et al*.[12] with 92.3%, 84.2%, 93.6%, 92.56%, and 89.6% cases respectively which is similar to our study with 96.67% of cases. Okoye[9] had slightly less proportion of cases probably because they included metastatic carcinoma in their study group unlike other studies.

In USA, a study by Adegoke *et al*.[13] for trends in cervical cancers for 35 years revealed that overall incidence of squamous cell cancer decreased annually between 1973 and 2007 by 8%, and the incidence of AdenoCa increased by an average of 2.9% per year over the same period. This reversal of trend is attributed to the fact that cervical screening programs consisting of mainly Papanicolaou smear examination has better sensitivity and specificity for squamous lesions compared to AdenoCa.

Adeniji[14] observed WDSCC (60.1%) as most common subtype whose study period was almost four decade earlier than the present study. There is a clinical correlation between the degree of differentiation of a tumor and its clinical behavior; well-differentiated tumors tend to be less aggressive than poorly-differentiated ones; however, this is not conclusively substantiated by studies yet.

Cancer of the cervix can develop in women of all ages. It usually develops in women aged 35–55 years with the peak age for incidence varying with populations; for instance, it is 30–40 years in UK and 35–39 years in Sweden (Cancer Research UK). In India, the peak age for cervical cancer incidence is 45–54 years, which is similar to the rest of South Asia.[15]

Among neoplastic lesions of cervix uteri, we made age parameter comparison with other studies [Table 2].

Thus, we observed that as the study period shifted to more recent times, detection peak of cervical cancers shifted from the 5th to 4th decade. This is possibly due to increased awareness among women regarding gynaecological problems as well as increased per capita income and better health-care facilities.

Clinical presentation of females with carcinoma as observed by Ikechebelu *et al*.[12] i.e., abnormal vaginal bleeding (postmenopausal/postcoital/abnormal spotting) was similar to present study.

With respect to cases with grand multipara, Ikechebelu *et al*.[12] observed majority in this category with mean gravida of 6.8 compared to 23.33% cases in the present study. Ikechebelu *et al*.[12] observed 89.3% cases in Stage III and IV compared to 42.2% of cases in the present study. This highlights the fact that cases presenting in late stages of carcinoma has a welcome decreasing trend due to various reasons such as better health-care facilities, accessibility, screening camps, increased awareness, and confirmatory histological diagnosis as well as better and early treatment by surgeons.

In conclusion, although the clinical presentation were more or less similar, the peak age presentation was a decade earlier than most of the studies (later half of the 4th decade versus 5th decade). Majority of cases were in Stage IIB (45.56%) followed closely by advanced Stage (III and IV) with 38.8%.

We observed that women were reluctant in approaching health clinics for gynaecological symptoms. Furthermore,

Table 2: Comparison of age parameters with other studies

Studies (place)	Time period	Age range	Peak decade	Mean age+SD
Adeniji[14] (Nigeria, Africa)	1979-1997	23-85	5th	51.8
Olu-Eddo *et al*.[8] (Benin, Africa)	1987-2006	15-90	5th	50.4+13.5
Okoye[9] (Nigeria, Africa)	2000-2009	18-99	5th	51.5+12.8
Jeebun *et al*.[16] (Mauritius, Africa)	2000-12	-	5th	50.6+10.6
Abudu *et al*.[10] (Olabisi, Africa)	2003-2004	31-70	4th	-
Pathak *et al*.[11] (Nepal)	2013	24-92	4th	42.5
Present study	2014-2015	22-75	4th	50.6+10.8

SD – Standard deviation

none of the cases had HPV vaccination before the first sexual encounter. Although awareness regarding the same is increasing, cost and social stigma are the main deterrent factors for females in the current scenario.

Early screening of the disease through cytology has considerably reduced morbidity and mortality from the disease in the developed world.[17] There is an urgent need for regular and effective cervical screening program in developing countries. HPV vaccination should be included in universal immunization program of India. Presently, due to the expensive HPV vaccine and limitations of cytology based screening programs owing to infrastructure, equipment and workforce -death and disability from this cancer are high in developing countries including India.[18]

Women being the main caretaker of children as well as an almost equal economical contributor in current era, needs to be properly screened for malignancies and detecting cases in the early stage of Cervical Intraepithelial Lesion will go a long way in reducing morbidity and mortality. Although there are many national programs successfully running for obstetrics cases, same is lacking for gynaecological problems.

The World Health Organization recommends that in low resource settings like ours, every woman should be screened at least once in her lifetime at 40 years. Frequency of screening should be increased to "once every 10 years" and then once every 5 years' for women 35–55 years of age. The frequency could be increased based on resources.[19] More research in the present context is needed so that best practices for the prevention and control of cervical cancer in Indian scenario can be developed and implemented.

Cervical cancer causes loss of productive life both due to early death as well as prolonged disability. In addition, the high medical costs incurred by families due to cervical cancer (especially since most cases in developing countries are diagnosed at advanced stages when treatment is costly but prognosis poor), further impoverish people.[20]

HPV infection and precancerous lesions go unnoticed and develop into full blown cancer before women realise they need to go for medical help.[21] HPV is a sexually transmitted infection, making cervical cancer a chronic disease with an infectious aetiology.[6] The main risk factor for the development of cervical cancer is HPV infection, DNA of which has been found in almost all cases of invasive cervical cancer in a study by Bosch and de Sanjosé[22] Atleast 50% of sexually active men and women get HPV once a lifetime.[23] Majority of females usually have self-resolving HPV infection which does not evolve into cancer cervix, however around 10% develop persistent infections, and are at high risk of developing cervical cancer.[24]

WHO recommends 9–13 year old girls who have not yet become sexually active as target group for HPV vaccination.[25] Schools may be targeted for giving better reach and coverage for future vaccination programs and will go a long way in reducing the burden of cervical lesions both nonneoplastic and neoplastic if implemented properly. Where school enrolment of girls is high, school-based vaccination is a possibility; however, different approaches are needed to reach girls not in school and who may be particularly vulnerable (e.g., street children, migrants). Attracting young girls to repeatedly come to health facilities and outreach sessions is likely to take special efforts.[25]

National educational campaigns for vaccine introduction should be used to increase community awareness about cervical cancer and its prevention. Designed messages are essential to educate communities, parents, teachers, adolescents about the HPV infection, vaccine and cervical cancer. Sex education is as important as vaccination and use of barrier methods goes a long way in protecting against all veneral diseases. Programs can be quickly undermined by misinformation if the reasons for targeting girls only are not fully and sensitively communicated. Educating men about HPV vaccines and cervical cancer is particularly important in a patriarchal society like ours. Involving mothers of young teenage girls and educating girls regarding advantage of screening procedures is another communication opportunity.[25]

In finance constrained setting like ours, cost of vaccine as well as operational cost for delivery also needs to be taken into consideration during planning process itself and will be a critical step in the decision-making process.

Due to difficulties of access and affordability, compliance and follow-up of treatment is much worse for women of low socioeconomic strata, leading to further morbidity and mortality from the disease. Despite the fact that early detection and treatment are one of the priorities of National Cancer Control Programme in India, yet there is no organized Cervical Cancer Screening Program in our country and same should be advocated and implemented at the earliest. We hope and recommend that this study will lay the foundation for policy makers to effectively prevent and control cervical lesions, especially cancers in the present and future scenario.

Conclusion

Cervical cancers pose a substantial burden on our social and health-care system. Although surgery and radiotherapy remains the mainstay of treatment, nothing can replace prevention and early detection of neoplastic cervical lesions. There is an urgent need for inclusion of HPV vaccination programs in Universal Immunization Program of India. Large scale screening programs for target populations should be organized to reduce the long term morbidity, mortality and socioeconomic burden related with cervical lesions. Furthermore, increasing literacy

rate, personnel hygiene, socioeconomic strata, and use of contraceptive measures to reduce parity will be highly instrumental in tackling the current and future burden of cervical cancers. Histomorphology remains the mainstay of diagnosis of cervical cancers. In low compliance settings such as ours, colposcopy-guided biopsy is the preferred course of management, especially in elderly females to be definite so as to rule out or diagnose neoplasia. National level cervical cancer program is immediate need of the hour and should include HPV vaccine, awareness and screening programs as well as treatment assistance for low socioeconomic strata. We recommend effective programs to be included in government health schemes to prevent and control cervical cancers in future as well as improve the present scenario.

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Conflicts of interest

There are no conflicts of interest.

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