MENOPAUSE AND CERVICAL CANCER- DESCRIPTIVE STUDY OF PRESENTATION AND MANAGEMENT IN TERTIARY CENTRE OF JHARKHAND, INDIA

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ABSTRACT

BACKGROUND

Cervical cancer is the most common genital cancer encountered in clinical practice in India. According to WHO there are 510,000 new cases every year with 80% occurring in developing nations, half of these cases end in death.¹ Cervical cancer accounts for 15% of all cancer in women. Menopause is a consequence of biological aging. Menopause itself do not cause cancer, but the risk of cancer increases as the women ages. Most studies on cervical cancer screening have focused on premenopausal women with little information provided on perimenopausal or postmenopausal women. However, these women remain at increased risk for cervical cancer given that there is a second peak in prevalence of high-risk HPV subtype in this oldest population.

The aim of the study was to determine the presentation as well as management of cervical cancer in postmenopausal women in Jharkhand.

MATERIALS AND METHODS

The descriptive study was conducted on postmenopausal females presenting in outpatient department, emergency and indoor patients admitted in the Department of Gynaecology and Obstetrics at Rajendra Institute of Medical Sciences, Ranchi, from March 2015 to September 2016. All postmenopausal women patients with suspected or proved cervical malignancy were included in the study.

RESULTS

The incidence of CIN (I + II + III) 8% and cervical cancer in this study was 16%. Maximum number of cases with cervical malignancy was in the age of 51 - 60 (45.83%). Postmenopausal bleeding (66.66%) was the commonest complaint present among cases of cervical cancer, while most common presenting complaint in postmenopausal women is related to postmenopausal syndrome i.e. backache, urinary symptoms; 77.08% cases of carcinoma was detected in advanced stage (stage IIb + III + IV). Average age of menopause in study population is 45 years.

CONCLUSION

Most cases in postmenopausal women were diagnosed at advanced stage, hence only radiotherapy was the treatment available. By improving cervical screening and awareness among women, it may be possible to detect cervical cancer in early stages so that preventive as well as curative treatment could be given.

KEYWORDS

Menopause, Cervical Cancer, Histopathology, Postmenopausal Bleeding.

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BACKGROUND

Cervical cancer is the second most common cancer in women worldwide and the most common cancer in developing nations. According to WHO, there are 510,000 new cases every year with 80% occurring in developing nations, half of these cases end in death.¹ Cervical cancer is considered a preventable disease by WHO, because it can be diagnosed in its precancerous phase. Data showed that in areas where screening has been carried out for a sufficient period of time,

which means 10 - 15 years, both the incidence and mortality of invasive cancer have been reduced.² Screening programme has proved successful in reducing the incidence of cervical cancer by 80% and its mortality by 60% in developed countries.

Most studies on cervical cancer screening have focused on premenopausal women with little information provided on perimenopausal or postmenopausal women. However, these women remain at increased risk for cervical cancer given that there is a second peak in prevalence of high risk HPV subtype in this oldest population. WHO defines menopause as permanent cessation of menstruation resulting from loss of ovarian activity. Common menopausal age in Indians is 45 - 50 years. Postmenopausal women constitute 1% of female population. HPV infection in older women is more likely to be persistent than transient, hence there is a need of regular screening in postmenopausal women to detect preneoplastic lesions. Older age allows accumulation of mutations that can lead to cellular malignancy. Transformation additionally decreased needs for prenatal care and contraception causes

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older women to access cervical cancer prevention programme less often.

So the consultation is an opportunity for health education and promotion for doctors. Patients need to be encouraged to utilise cervical screening programmes. It is also important to remember that cervical cancer can present with non-specific symptoms, thus the onus is on all doctors to take a good history and perform a thorough examination. Failing to do so may delay making the right diagnosis with associated morbidity and mortality.³ According to Andrae B, Andersson TM, Lambert PC, et al screening is associated with improved cure of cervical cancer. Evaluations of screening programmes should consider the assessment of cure proportions.⁴ As with many other types of cancer, the outcome depends on how advanced the cervical cancer is when it is diagnosed. In other words, the stage of the cancer.

As per National Institute of Cancer Prevention and Research (NICPR)- One woman dies of cervical cancer every 8 minutes in India. In India, cervical cancer was the third largest cause of cancer mortality in 2004.⁵ The current estimates indicate approximately 132,000 new cases diagnosed and 74,000 deaths annually in India, accounting for nearly 1/3rd of the global cervical cancer deaths.⁶ There are currently several cervical cancer research programmes in India. The National Cancer Registry Programme, established by the Indian Council of Medical Research, acts as a surveillance system for cancer in India. Management of cervical cancer in postmenopausal women need special consideration, as they seek treatment in an advanced stage of disease because of other associated diseases and dependency. They always need examination under general anaesthesia. Pap smear screening in postmenopausal women is inaccurate and often negative on account of dry vagina, poor shedding of cervical cells or in drawing of squamocolumnar junction.

These are the women who have many other comorbid conditions like hypertension, diabetes, cardiac problems and cerebrovascular problems, hence require better preop, intraop as well as postop management. Hence, may need referral to higher specialised centre. Many of these were found to be unfit for major surgery as well as radiotherapy. Thus, management protocol which are well suited in premenopausal might not help in old age. Hence, these patients need special attention. The aim of the study was to determine the presentation as well as management of cervical cancer in postmenopausal women in Jharkhand.

MATERIALS AND METHODS

The descriptive study was conducted on postmenopausal females presenting in outpatient department, gynaecology emergency and indoor Department of Gynaecology and Obstetrics from March 2015 to September 2016. Total 300 postmenopausal women patients with suspected or proved cervical malignancy, who gave proper informed written consent were included in the study. Symptoms proved to be due to obvious non-gynaecological cause and women who had not attained menopause were excluded.

Details regarding the patients such as age, parity, presenting symptoms were recorded. Complete assessment was done by history, clinical examination and investigations which included Pap smear, transvaginal ultrasound, diagnostic hysteroscopy and endometrial and/or cervical

biopsy. Pap smear is a screening test only. Positive test requires further investigations like colposcopy, cervical biopsy and fractional curettage. Pap smear can detect 98% of cancer of the cervix. Biopsy is essential in every case where signs or symptoms raise the slightest suspicion and it is irrespective of whether cervical smear contain malignant cells. Biopsy was taken from abnormal area, in the form of either a cervical punch or wedge or cone biopsy in operation theatre under anaesthesia. The specimen was sent for histopathological examination in 10% formalin solution. Histopathological evaluation of biopsy specimens were conducted by Pathology Department of Rajendra Institute of Medical Sciences, Ranchi, Jharkhand.

RESULTS

This descriptive study was conducted from March 2015 to September 2016 in Department of Obstetrics and Gynaecology, Rajendra Institute of Medical Sciences. During this period, all the postmenopausal patients who attended Gynaecology OPD, Gynaecology emergency or admitted in indoor of Rajendra Institute of Medical Sciences (Gynaecology and Oncology) were included in the study except those having some obvious non-gynaecological cause. Total number of patients who fulfilled the inclusion criteria were 368, but only 300 patients gave informed written consent. Postmenopausal patients considered were those with amenorrhea of at least 1 year. All patients in the study were more than forty years of age.

In the present study, the maximum age at presentation was 75 years and the minimum age at presentation was 43 years. The patients were divided into four groups based on the age at clinical presentation. Maximum number of patients were observed in the age range of 41 - 50 years and minimum number in the age range of 71 - 80 years.

The Fig. 1 shows distribution of the patients in different age groups. Maximum patients were in the age group in 41 - 50 yrs. (43.33%). Minimum patients were in the age group in 71 - 80 yrs. (3.33%).

Figure 1. Distribution of the Patients according to different Age Group

Considering the age at menopause, minimum age at menopause in our study population was 40 years and maximum age at menopause was 54 years. The mean age at menopause was 45 years.

Figure 2. Presenting Complaints among Postmenopausal Women

Majority of the patients presented with more than one complaint were chalked out separately and the number of patients under each complaint were calculated.

Presenting Complaint	No. of Patients	Percentage (%)
Postmenopausal bleeding	32	66.66
Watery discharge per vaginum	20	41.66
Blood stained discharge	20	41.66
Contact bleeding	06	08.33
Something coming out per vaginum	07	04.16
Foul smelling discharge	15	31.25
Pain in lower abdomen, backache	28	58.33

Table 1. Presenting Complaint among Carcinoma Cervix Cases

Most of the patients had more than 1 complaint, postmenopausal bleeding was the commonest complaint present in 66.66%. Second most common complaint was of lower abdomen pain in 58.33% of cases and then watery and blood mixed discharge per vagina in 41.66% of cases.

In the present study in 37 out of 48 (77.1%) cases, the duration of complaint was more than 6 months.

Findings	No. of Cases	Percentage
Inflammatory/ metaplasia	136	45.33
ASCUS	6	2
CIN I	6	2
CIN II/ CIN III	18	6
Invasive Carcinoma	48	16

Table 2. Final Histopathological Findings

Stage	No. of Cases	Percentage (%)
I A	0	00.00
I B	7	14.58
II A	4	08.33
IIB	13	27.08
III A	4	08.33
III B	18	37.50
IV A	2	04.16
IV B	0	00.00

Table 3. Cases according to Clinical Staging

We see that 11 patients (20.91) out of 48 presented as stage IB or IIA cancer cervix. Maximum patients 37 (77.08%) came under advanced stage (stage IIb + III + IV).

Gross Appearance of Lesion	No. of Patients	%
Cauliflower like growth	30	62.50
Ulcerative or excavating type	9	18.75
Erosion cervix	5	10.41
Barrel-shaped cervix	4	08.33
N=48		

Table 4. Distribution of Cases according to Macroscopic Pattern of Growth

Cauliflower like growth is the most common presentation. Endocervical growth of the cervix is expanded and becomes barrel shaped.

Histological Type	Number of Cases (%)
Squamous cell carcinoma	43(89.58%)
Adenocarcinoma	4(8.33%)
Clear cell carcinoma	1(2.08%)

Table 5. Case according to Histopathological Type of Cancer Cervix

Sq. Cell Carcinoma		Adenocarcinoma	
Grade	No. of Patients Percentage (%)	Differentiation	No. of Patients Percentage (%)
Grade I	2 (4.60%)	Well	1(25%)
Grade II	35 (81.39%)	Moderately	2(50%)
Grade III	5 (11.62%)	Poorly	1(25%)
Grade IV	1 (2.30%)		
n=43		n=4	

Table 6. Case of Epidermoid (Squamous Cell), Adenocarcinoma according to Degree of Differentiation. (Broders' Classification)

Modes of Treatment	No. of Patients	Percentage (%)
Radical surgery (Wertheim's hysterectomy)	3	4.16
Radiotherapy	31	72.91
Wertheim's hysterectomy + post-operative radiotherapy	6	6.25
Chemotherapy + RT	8	16.66

Table 7. Distribution of Cases of CA Cervix according to Modes of Treatment

Out of 11 cases (IB + IIA), 3 patients had radical hysterectomy and 6 patients had radical hysterectomy followed by radiotherapy. One patient was diagnosed as stage IB, but when abdomen was opened the uterus was found to be fixed, posterior abdomen closed and later on patient was referred for radiotherapy. Majority of the patients, 31 out of 48, received radiotherapy as first line of treatment. Pelvic lymph node removed in all cases was sent for histopathological examination.

DISCUSSION

In our study out of 300 patients, 136 patients were in 41 to 50 years' age group (as per Fig. 1). This shows relatively better health in this age group compared to others. The number of patients in higher age groups gradually decreased probably due to their poor health status and their dependence on

others for seeking health facility. Only 10 patients in age group 71 - 80 years reached for treatment, which comprises of only 3.3% of total. This also indicates poor survival apart from poor health and dependence in this age group.

The average age of menopause in present study is 45 years. Our study has similarity with a recent study conducted "A PAN India survey by IMS" in the year 2016, which showed the mean age of menopause in Indian women is 46.2 years.

Fig. 2 demonstrates the symptom wise presentation of study patients. This shows that most of the patients (162) presented with lower backache, which is non-specific symptoms followed by urinary complaints (122). The third common complaints were either bleeding per vagina or prolapse or vaginal discharge. Thus, the majority of patients were not aware of having significant gynaecological problem initially, but subsequently their symptoms were found to have related with one or the other gynaecological morbidity. Cervicitis and pelvic inflammatory disease may be the cause of backache and urinary symptoms in these patients. Backache, urinary symptoms in these postmenopausal women can also be due to decreased oestrogen.

Cervical Malignancy

In our study, 136 cases out of 300 (45.33%) cervical smear showed inflammatory changes which suggests that cervicitis is the most common disease diagnosed in postmenopausal group. This may be the possible reason for backache in this population. A course of antibiotic was given to these cases and repeat smear was done after treatment; 2% cases had ASCUS and 2% CIN I. These were followed up at regular interval. Majority of CIN 2/CIN 3 patients were managed by hysterectomy, few cases in this group were treated by cryosurgery. In the present study, the overall incidence of CIN reported by Pap smear was 8%. The overall incidence of CIN on cytology was 7.75% reported by Bhojani KR et al (2011)⁷ and 8.2% by Bukhari et al (2012)¹⁰.⁸ Thus, our result is very similar to these results.

The increased incidence of CIN and malignancy was also due to low literacy rate and low socioeconomic status, lack of health awareness in rural setup along with inaccessibility of proper health care facilities being a cause of neglecting the symptoms in the preclinical stage of cervical cancer.

During the study period, a total of 48 patients were confirmed to have cervical malignancy among total 300 study subjects. Thus, the incidence of cervical carcinoma in our study was 16%.

Study	Year	Cancer Cervix
Sengupta A ⁹ , et al	1990	32%
Naik VS ¹⁰ et al	2004	39.4%
Kothapally K ¹¹ et al	2013	10%
Present Study	2016	16%

Table 8. Comparing Frequency of Malignancies in various Studies

The disparity between the results of the present study and other studies may be due to selection of only postmenopausal women as cases who had positive symptoms, signs and cervical pathology in the present study, whereas in most of the other studies mentioned above only mass screening procedures were adapted.

27 out of 48 (i. e. 56.25%) were diagnosed to have cervical malignancy in OPD or indoor by just proper clinical

examination. But directly or indirectly all of them were subjected to tissue diagnosis. Pap smear and cervical biopsies played important role and 10 cases were diagnosed by each of them. In 10 patients when Pap smear was done it showed HSIL, but cervical biopsy report was suggestive of squamous cell carcinoma. This disparity reveals that cervical biopsy is a must for diagnosis. Only one patient presented to us with a positive histopathology for cervical carcinoma following hysterectomy. As per cancer survivor reports, only a good history with meticulous clinical examination is enough for diagnosis of carcinoma cervix in most of the cases. This supports our study. The maximum positive cases were in age group 51 - 60 years (22/48, i.e. 45.83%) followed by 41 - 50 years (16/48, i.e. 33.33%). The incidence was lesser in higher age group, which may be related to lesser number of participants in those groups due to mortality and dependence.

Table No. 1 shows the presenting complaints among the cases of carcinoma cervix. The commonest complaints was postmenopausal bleeding, which was present in 32 (66.66%) cases. The second common complaints were blood stained discharge and water mixed discharges. Each complaint was seen in 20 (41%) cases, while 7 (14.58%) patients presented with something coming out per vagina (prolapse). Anorlu RI, Orakwue CO et al in their study on 127 patients found results very similar to our study, in this study 127 patients with a mean age of 54.6 +/- 13.4 years. Common symptoms at onset of disease were postmenopausal bleeding (55.9%) and vaginal discharge (48.8%). Of the patients, 60.71% first went to private hospitals. The interval between onset of symptoms and seeking healthcare was 6.10 +/- 9.31 months; time elapsing between seeking healthcare and referral to a tertiary hospital was 9.35 +/- 12.9 months. Stage 3A cervical cancer was diagnosed in 71.8%.

Most of the patients (28/48, i.e. 58.33%) present between 6 months to 1 year of symptoms. This delay of presentation may be due to the fact that bleeding and discharge are common complaints and most of the gynaecological diseases present with these complaints only. Also, the delay of presentation may be due to the poor social status of these females.

Table No. 3 (A and B) show the clinical stages at presentation among the positive cases in our study. In our study, maximum cases presented in advanced stages either IIB (27. 08%) or IIIB (37. 50%). Categorisation of patients in early and advanced disease shows that 11 (22.91%) cases presented in early stage of their disease, while remaining 37 (77. 09%) presented with advanced form of cancer.

In the year 2004, Anorlu RI, Orakwue CO and Oyeneyin L et al in their study concluded that patient's delay in seeking healthcare and care provider's delay in referring patients to a tertiary hospital contributed to the late presentation.

The gross appearances of cervix revealed cauliflower-like growth in 30 (62. 50%) followed by ulcerative or excavating type 9 (18.75%). Also Erosion of cervix is seen in 5 (10.41%) cases and Barrel shaped cervix in 4 (08.33%) cases, (Table No. 4). As per conventional studies, fungating/exophytic growth is the commonest macroscopic presentation of cervical carcinoma.

Table 5 shows the case according to histopathological type of cancer cervix and squamous cell carcinoma in 43 (89.58%), adenocarcinoma in 4 (8.33%) and clear cell

carcinoma in 1 (2.08%) patient. Hence among the study cohort, maximum number of patients had squamous cell carcinoma. In a study by south India by Kulkarni and Kulkarni reveals that multiple infection of HPV 16 and 18 is quite high in cervical cancer and especially in squamous cell carcinoma. Hence, considering the possibility of promotion of persistence of non-vaccine types in the vaccines due to original antigenic sin and the lack of organised screening programs in India, a broad-based vaccine approach would be appropriate.

Table 6 shows the case of epidermoid (squamous cell) carcinoma according to degree of differentiation. According to this table, maximum number of patients presented had grade II (35/43, i.e. 81.39%) followed by grade III (5/43, i.e. 11.62%) squamous cell carcinoma. Adenocarcinoma was categorised into well differentiated, moderately differentiated and poorly differentiated which were 1, 2 and 2 in number respectively. In a cross-sectional study by Ndlovu N, Kambarami R et al under heading "Factors associated with tumour stage at presentation in invasive cervical cancer" says that 80% cervical carcinoma presented with late stage disease. Squamous cell carcinoma was the commonest histology (96%) with adenocarcinoma constituting only 4% of all tumours. Poorly differentiated tumour histology and no history of prior cervical cancer screening were found to be significantly associated with late tumour stage at presentation.

Table No. 7 shows the mode of treatment to the conformed cases of cervical carcinoma in study. In our study, maximum number of patients referred for radiotherapy (72.91%). Only 4% cases underwent radical surgery (Wertheim's hysterectomy) and Wertheim's hysterectomy + postoperative radiotherapy done in 6.25% patients. Chemotherapy + RT was done in 8 patients, which consists 16.66% of total positive cases. Most of the patients presented late, hence option of surgery was not acceptable. The best management of stage IB and early stage of IIA remains controversial, but there is evidence that either radical hysterectomy or radiotherapy will cure 90% - 90% of these tumours.

CONCLUSION

Cancer of the uterine cervix is the commonest cancer among Indian women accounting for 20% of the total cancer incidence in Indian population. Present study was conducted at Rajendra Institute of Medical Sciences, Ranchi, for a period of 1-½ years. During the study period, 300 postmenopausal women were enrolled from Department of Gynaecology (OPD, Emergency) and Department of Oncology. The patients were thoroughly examined and evaluated to look for the incidence of disease, varied presentations and management in postmenopausal women evaluated.

In our study, mean age of menopause was 44.5 years. Mostly, postmenopausal women visit hospital because of backache and urinary symptoms. The commonest presenting complaint among positive cases were postmenopausal bleeding (66.66%), while watery discharge, blood mixed discharge, something coming out of vagina and contact bleeding were also important complaints. The incidence of cervical carcinoma was 16% among the total postmenopausal women enrolled in the study during study period. Most of the carcinoma cases presented in advanced stage, hence only radiotherapy was advised.

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