

Retrospective histopathological analysis of various neoplasms of the female reproductive system (FRS) seen at the Kathmandu University Teaching Hospital, (KUTH) Dhulikhel, Nepal

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Abstract

Objective: To find out the spectrum of various histopathological types of primary neoplasms of different parts/organs of the female reproductive system seen at the Kathmandu University Teaching Hospital (KUTH) as there exists a worldwide wide variation in the distribution of various neoplasms, which appears largely due to exogenous factors rather than due to inherent differences between populations.

Material and Method: This was a retrospective study. It was carried out at KUTH. All neoplasms of the female reproductive system seen at the KUTH during the period of 20 months from 1st January 2004 to 31st August 2005 were included in this study and examined by light microscope (LM).

Results: A total number of 60 cases of neoplasms of the female reproductive system were seen. Out of these, 1 (1.7%) was of the vagina (squamous cell carcinoma, papillary variant); 16 (26.7%) were of the cervix of the uterus (all squamous cell carcinoma in advanced stage); none were of the endometrium; 20 (33.3%) were of the body of the uterus/uterine muscle (all leiomyomas); 16 (26.7%) were of the ovary, (11 benign, consisting of nine mature cystic teratoma, also known as dermoid cyst, one serous papillary cystadenoma and one mucinous cystadenoma; and, five malignant, consisting of two serous cystadenocarcinoma, two mucinous cystadenocarcinoma and one mixed mucinous and serous cystadenocarcinoma); and, 7 (11.6%) were of the breast (two benign, consisting of fibroadenoma and five malignant, all consisting of infiltrating ductal carcinoma in advanced stage).

Conclusion: There were relatively a large number of cases of advanced stage of cancer of uterine cervix. All breast cancers seen were also in advanced stage. Endometrial carcinoma was conspicuously absent in our this small series of cases.

Key words: Neoplasms, female reproductive system (FRS), Kathmandu University Teaching Hospital (KUTH)

There is a worldwide wide variation in the distribution of various neoplasms. These international differences appear largely due to exogenous factors rather than due to inherited differences between populations.¹ On a global basis out of the first eight ranking cancers in females, the cancers of the female reproductive system rank as follows: 1st breast, 2nd cervix of the uterus, 7th ovary; and, 8th body of the uterus [3rd being colon/rectum, 4th stomach, 5th lung; and, 6th oral cavity]². This study was done to find the relative frequency of various histopathologic type of neoplasms of the female reproductive system seen at KUTH, Dhulikhel in comparison to the worldwide distribution.

Materials and methods

This was a retrospective study. It was carried out at KUTH. All cases of various neoplasms of different parts/organs of the female reproductive system that were submitted to the histopathologic laboratory

during the period of 20 months from 1st January 2004 to 31st August 2005 were included in this study, and examined by light microscope (LM).

Results

A total number of 60 cases of neoplasms of the female reproductive system were seen. Out of these, 1 (1.7%) was of the vagina (squamous cell carcinoma, papillary variant); 16 (26.7%) were of the cervix of the uterus (all squamous cell carcinoma in advanced stage); none were of the endometrium; 20 (33.3%) were of the body of the uterus/uterine muscle (all leiomyomas); 16 (26.7%) were of the ovary, (11 benign, consisting of nine

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mature cystic teratoma, also known as dermoid cyst, one serous papillary cystadenoma and one mucinous cystadenoma; and, five malignant, consisting of two serous cystadenocarcinoma, two mucinous cystadenocarcinoma and one mixed

mucinous and serous cystadenocarcinoma); and, 7 (11.7%) were of the breast (two benign, consisting of fibroadenoma and five malignant, all consisting of infiltrating ductal carcinoma in advanced stage) (Table - 1).

Table 1. Part/Organ- wise distribution of neoplasms of the female reproductive system (FRS)

Parts of FRS	No. of cases (%)	Histopathologic type
Vagina	1 (1.7)	Squamous cell carcinoma, papillary variant
Uterine cervix	16 (26.7)	All squamous cell carcinoma
Uterine body	20 (33.3)	All leiomyomas
Ovary	16 (26.7)	9 mature cystic teratomas, 1 serous papillary cystadenoma, 1 mucinous cystadenoma, 2 serous adenocarcinoma, 2 mucinous adenocarcinoma and 1 mixed mucinous and serous cystadenocarcinoma
Breast	7 (11.7)	2 fibroadenoma and 5 infiltrating ductal carcinoma
Total	60	

Of all the neoplasms, the total number of benign cases were 33 (55%); and, malignant were 27 (45%). Part/organ -wise distribution of benign vs. malignant cases was as follows: Vagina - benign none, malignant one case (squamous cell carcinoma, papillary variant); uterine cervix - benign none; malignant all of the 16 (all squamous cell carcinoma, advanced stage) cases; uterine muscle - benign all of the 20 cases (all leiomyomas), malignant none; ovaries - benign 11 cases (9

mature cystic teratomas, dermoid cyst, 1 serous papillary cystadenoma, and 1 mucinous cystadenoma), malignant 5 cases (2 serous cystadenocarcinoma, 2 mucinouscystadenocarcinoma and 1 mixed mucinous and serous cystadenocarcinoma); and, breast - benign 2 cases (both fibroadenomas) and malignant 5 cases (all infiltrating ductal carcinoma in advanced stage) (Table – 2).

Table 2: Benign vs. malignant neoplasms of female reproductive system (FRS)

Parts of FRS	Benign (%)	HP type	Malignant (%)	HP type	Total (%)
Vagina	0		1 (1.7)	SCC	1 (1.7)
Uterine cervix	0		16 (26.7)	SCC	16 (26.7)
Uterine body	20 (33.3)	Leiomyomas	0		20 (33.3)
Ovary	11 (18.3)	9 DC 1 MCA 1 SCA	5 (8.3)	2 SCACa 2 MCACa 1 Mixed	16 (26.7)
Breast	2 (3.3)	FA	5 (8.3)	IDCa	7 (11.6)
Total	33 (55)		27 (45)		60 (100)

HP type = Histopathologic type
 SCC = Squamous cell carcinoma
 DC = Dermoid cyst
 MCA = Mucinous cystadenoma
 SCA = Serous cystadenoma
 SCACa = Serous cystadenocarcinoma
 MCACa = Mucinous cystadenocarcinoma
 FA = Fibroadenoma
 IDCa = Infiltrating ductal carcinoma

The overall age distribution was : 10-20 years 4 cases (Benign 4: 2 dermoid cysts of the ovary, 1 serous papillary cystadenoma of the ovary, 1 fibroadenoma of the breast), 21 to 30 years 8 cases (Benign 5, Malignant 3: 2 squamous cell carcinoma

of uterine cervix, 2 leiomyomas of the uterus, 1 dermoid cyst of the ovary, 1 mucinous cystadenoma of the ovary, 1 mixed mucinous and serous cystadenocarcinoma of the ovary, 1 breast fibroadenoma), 31 to 40 years 15 cases (Benign

11, Malignant 4: 3 squamous cell carcinoma of uterine cervix, 7 leiomyomas of the body of the uterus, 4 dermoid cysts of the ovary and 1 infiltrating ductal carcinoma of the breast), 41 to 50 years 20 cases (Benign 12, Malignant 8: 4 squamous cell carcinoma of uterine cervix, 10 leiomyomas of the body of the uterus, 2 mucinous cystadenocarcinoma of the ovary, and 2 dermoid cysts of the ovary, and 2 infiltrating ductal carcinoma of the breast), 51 to 60 years 9 cases (Benign 1, Malignant 8: 1 squamous

cell carcinoma of the vagina, papillary variant, 4 squamous cell carcinoma of the uterine cervix, 1 leiomyoma body of uterus, 1 serous cystadenocarcinoma of the ovary, 2 infiltrating ductal carcinoma of the breast), 61 to 70 years 4 cases (All Malignant: 3 squamous cell carcinoma of uterine cervix, 1 serous cystadenocarcinoma of the ovary) (Table – 3).

Table 3. Age-wise distribution of the neoplasms of the female reproductive system (FRS)

Parts of FRS	10-20	21-30	31-40	41-50	51-60	61-70	Total
Vagina (All M)	0	0	0	0	1	0	1
Uterine cervix (All M)	0	2	3	4	4	3	16
Uterine Body (All B)	0	2	7	10	1	0	20
Ovary B/M	3 B3	3 B2/M1	4 B4	4 B2/M2	1 M1	1 M1	16
Breast B/M	1 B1	1 B1	1 M1	2 M2	2 M2	0	7
Total	4	8	15	20	9	4	60

B = Benign; M = Malignant

Discussion

On a global basis out of the first eight ranking cancers in females, the cancers of the female reproductive system rank as follows: 1st breast, 2nd cervix of the uterus, 7th ovary; and, 8th body of the uterus--3rd being colon/rectum, 4th stomach, 5th lung; and, 6th oral cavity.² However, neoplasms of various parts/organs of the female reproductive system (FRS) have a marked international variation of distribution according to the parts/organs of the FRS affected. The incidence of cancer in 1996 in developed world in thousands was: breast 494, cervix of the uterus 102, body of the uterus 104, ovary 91. In comparison, in the developing world it was 416, 421, 68 and 100 respectively.² These international variations appear largely due to exogenous factors rather than due to inherited differences between populations.¹ Furthermore, these epidemiologic contrasts must contain causative clues that remain to be deciphered. The knowledge of these exogenous factors with possible causative clues should help in better management/prevention of these diseases worldwide as well as here in Nepal. The occurrence of various neoplasms affecting different parts/organs of the FRS worldwide in comparison to the cases seen in our present study at KUTH are discussed below.

Neoplasms of the Vagina

Primary carcinoma of the vagina is an extremely uncommon cancer (about 0.6 per 100,000 women yearly) accounting for about 1% of malignant neoplasms in the female genital tract, and of these, 95% are squamous cell carcinomas. Most are associated with HPV (Human Papilloma Virus). The greatest risk factor is a previous carcinoma of cervix or vulva; 1% to 2% of patients with an invasive cervical carcinoma eventually develop a vaginal squamous carcinoma.³ In our study, we had one case of cancer of the vagina that was squamous cell carcinoma, papillary variant. This patient, a 51-year-old woman, had history of squamous cell carcinoma of the uterine cervix and had had transabdominal hysterectomy with bilateral salpingo-oophorectomy, chemotherapy; and, radiotherapy.

Neoplasms of the cervix of the uterus

Cancer of the uterine cervix is surpassed only by breast cancer as the most common cause of cancer mortality among women worldwide and it is the most common incident cancer among women in developing countries. In the United States, incidence rates of invasive cervical cancer have declined steadily over the past few decades,

whereas these rates continue to rise in many developing countries.¹ In 1996 in developed world the incidence of carcinoma of the uterine cancer was 102,000 whereas in sharp contrast in the developing world it was 421,000.² This has led to the development of etiologic hypotheses implicating inadequate hygienic conditions and infrequent utilization of barrier contraception methods.¹ Furthermore, in the United States, the decrease in the incidence rate of cancer of the uterine cervix during the last several decades is presumably as a result of the widespread use of cervical cytologic screening [Papanicolaou smear screening (PAP)] programs.⁴ The reason that Papanicolaou smear screening (PAP) is so effective in preventing cervical cancer is that the majority of cancers are preceded by a precancerous lesion. This lesion may exist in the noninvasive stage for as long as 20 years and shed abnormal cells that can be detected on cytologic examination.³

In our series there were relatively a large number of cases of advanced stage of the carcinoma of the uterine cervix. This could be due to several factors such as lack of early detection due to inadequate screening facilities, women not participating in these screening programs, false negative rate during screening. Al-Nafussi et al found in their study that cervical smears may give false negative results, as seen in 35%, 18% and 3% of their cases of CIN 1, CIN 2, and CIN 3 respectively.⁵

Additionally, this could be due to high rate of occurrence of cancer of the uterine cervix, which could possibly be due to various factors such as poor socio-economic conditions. Also, there is evidence that tobacco smoking increases the risk for cervical cancer.¹ This could be one of the contributing factors, since in Nepal according to estimation by WHO 28.7% of females above 15 years of age smoke.⁶ Larger prospective studies should help in throwing more light on this serious health problem, thereby, providing guidelines for better management/prevention of this deadly disease in Nepal.

Neoplasms of the body of the uterus and endometrium

Uterine leiomyomas are perhaps the most common tumour in humans. These benign tumours may be present in about 75% of females of reproductive age.³ Similar to this, we found 20 cases of leiomyomas, which accounted for 33.3% of all neoplasms of the FRS in our series.

Carcinoma of the endometrium is the most common gynaecologic malignancy in developed countries.⁷ Worldwide, of all the malignancies of the female reproductive system, it ranks fourth in frequency after breast, uterine cervix and ovary.² Obesity, hypertension, diabetes mellitus, breast cancer, conditions that predispose to unopposed estrogen (i.e., absence of ovulation and therefore no periodic progesterone), and a family history of breast or ovarian cancer are possible predisposing factors.⁸

In our series, there were no cases of endometrial cancer found. This could possibly be due to low prevalence of the risk factors such as obesity, diabetes, hypertension etc. Further studies are necessary to explore this.

Another contributing factor could be high rate of smoking in Nepalese women⁶ as there is evidence that tobacco smoking reduces the risk for endometrial cancer. Smokers tend to have lower oestrogen levels and to be leaner than non smokers.¹

Neoplasms of the ovary

Tumours of the ovary are common forms of neoplasia in women. Among cancers of the female reproductive system, the incidence of ovarian cancer ranks below only carcinoma of the breast and uterine cervix.² Ovarian cancer accounts for 6% of all cancers in the female. However, because many of these ovarian neoplasms cannot be detected early in their development, they account for a disproportionate number of fatal cancers, being responsible for almost half of the deaths from cancer of the female genital tract.

Risk factors for ovarian cancer are much less clear than for other genital tumours.³ Despite some 30 epidemiologic studies of ovarian cancer, the causes of disease remain poorly understood. New hypotheses as to the cause need to be considered.

There are numerous types of ovarian tumours, both benign and malignant. The majority of ovarian cancers are epithelial carcinomas.¹ About 80% are benign, and these occur mostly in young women between the ages of 20 and 45 years. The malignant tumours are more common in older women between the ages of 40 and 65 years.

In our series there were 16 cases of neoplasms of the ovary. Out of these, 11 were benign and five were malignant. Of the 11 benign neoplasms, nine were mature cystic teratomas (dermoid cysts). The age range for this was between 13 years to 40 years. Of the two other benign neoplasm, one was serous papillary cystadenoma in a 20-year-old female; and, the other was mucinous cystadenoma in a 22-year-old female.

Out of the five malignant neoplasm of the ovary, two were serous cystadeno-carcinoma, two were mucinous cystadenocarcinoma; and, one was mixed mucinous and serous cystadenocarcinoma. The age range was from 27 years to 65 years.

Neoplasms of the breasts

Breasts or mammary glands are the soul of motherhood and the core of the evolution of mammals, such that can be aptly expressed in the dictum: No mammary glands, no mammals. However sadly, breasts are very susceptible to develop cancer. Breast cancer is the most common non-skin malignancy in women and has the highest fatality rate of all cancers affecting women.

Breast cancer incidence rates in the United States and Europe are four to seven times higher than those in other countries. The risk of breast cancer increases in immigrants to the United States during several generations. The specific factors for this phenomenon have not been identified.⁹

Breast cancer is the most common cause of death in middle-aged women in Western countries and is therefore, thought that dietary factors may play a role in its causation. There is some evidence that there is a link between diets low in phytoestrogens. It is known that in post-menopausal women, breast cancer is more common in the obese. This is thought to be because of an increased conversion of steroid hormones to oestradiol in the body fat.¹⁰

In our series there were seven cases of breast neoplasms. Out of these, two were benign (fibroadenomas), one in a 18-year-old and the other in a 21-year-old woman. Five were malignant, all of which were infiltrating ductal carcinomas in late stage. The age of these patients was 35, 47, 50, 51 and 52 respectively.

Khan et al¹¹ and Yadav et al¹² found in their study of diseases of breast in Nepal that patients with breast cancer presented themselves in very late stage of the disease. The reason for this in

Nepal is thought to be due to lack of knowledge about consequences of breast lump and also patients are shy to show their breast lump to doctor, unless it is very painful or ulcerated. Also, in early stages they go to “Hakims” and come to hospital only in late stage. To improve this situation they suggest establishment of special breast clinics in hospitals. Such clinics should also be involved in the early detection programs through newspaper or electronic media and also, educate women in regular self-examination of the breast, as more than 80% of breast cancers are discovered as a lump found by the patient herself.⁸

Conclusion

In our this small series of various neoplasms of different parts/organs of the female reproductive system, relatively a large number of cases of advanced stage of the carcinoma of the uterine cervix were found. More community oriented work including PAP smear and education might help in reduction of the incidence of this preventable deadly disease. Also, all the cases of breast cancer found were seen in late stage. Again, community education, including self-breast examination and seeking medical help for breast lumps sooner than later might help in reducing breast cancer related morbidity and mortality. No cases of cancer of the endometrium were found in our study. Further larger study needs to be done for collaboration/confirmation of this finding. Should the larger study also reveal similar findings, then possible contributing factors for this phenomenon need to be sought and encouraged to maintain this. Although the number of neoplasms in our this series was relatively low, yet we were able to get a sense of the spectrum of various histopathologic types of primary neoplasms arising from different parts/organs of the female reproductive system. Nonetheless, larger case studies are needed to confirm our findings. Furthermore, the current knowledge certainly points to significant contribution by environmental factors worldwide in the development of various neoplasms of different parts/organs of the FRS, particularly of the uterine cervix and breasts. Prospective studies focused on this might help in deciphering the environmental factors responsible for the etiopathogenesis of these deadly diseases.

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