Original Research Article

Journal of College of Medical Sciences-Nepal, Vol-19, No 1, Jan-Mar 2023
ISSN: 2091-0657 (Print); 2091-0673 (Online) Open Access
DOI: 10.3126/jcmsn.v19i1.52017

Histopathological Spectrum of Neoplastic Lesions of Female Reproductive System at a Tertiary Care Hospital in Bharatpur, Chitwan

Mamata Sedhain,[1] Priya Pathak,[2] Binita Goyal,[1] Pratigya Subedi[1]

[1]Department of Pathology, [2]Department of Community Medicine, College of Medical Sciences, Bharatpur, Chitwan, Nepal.

ABSTRACT

Introduction

Malignant neoplasms of the female genital tract accounts for majority of the cancers in females. The incidence and pattern of malignancies vary from region to region due to differences in genetic patterns, lifestyle and sociocultural factors. The objective of this research is to study the histopathological spectrum of neoplastic lesions of female reproductive system.

Methods

A total of 309 samples of neoplastic lesions were included in the study from the period of January 2017 to December 2021.

Results

Most of the neoplastic lesions were found in the uterine corpus, followed by ovary, breasts, cervix and vulva. 80.25% of the neoplastic lesions were benign and 11.97% were malignant; the rest being premalignant and borderline categories.

Conclusions

Malignant neoplasms of female genital tract contributes to major cancer burden among women and therefore special measures should be adopted to reduce its incidence and improve the prognosis.

Keywords: cervix; neoplasms; ovary; prognosis.

INTRODUCTION

According to the World Health Organization, the global cancer burden has increased to 18.1 million new cases and 9.6 million deaths in 2018.[1] On a global basis, out of the first eight ranking cancers in females, the cancers of female reproductive system rank as follows: 1st breast, 2nd uterine cervix, 7th ovary and the 8th being body of uterus.[2-5]

The incidence and pattern of malignancies of the female reproductive tract is known to vary from region to region because of the differences in genetic patterns, lifestyles, environmental, socio-cultural and economic factors.[5] Histopathological

Correspondence: Dr. Mamata Sedhain, Department of Pathology, College of Medical Sciences, Bharatpur, Chitwan, Nepal. Email: mamta15sedhain@gmail.com. Phone: +977-9860920786.

examination is mandatory for confirmation of clinical diagnosis, correct categorization and further staging of tumor. [1]

Thus this study intends to study the histopathological spectrum of neoplastic lesions of the female reproductive system and find out its frequency distribution in different anatomical sites.

METHODS

A retrospective cross sectional study was conducted in the department of Pathology at College of Medical Sciences, Bharatpur, Chitwan from the period of January 2017 to December 2021. Ethical clearance was obtained from the College of Medical Sciences Teaching Hospital-Institutional Review Committee (COMSTH-IRC) (Ref No.2022-15-01). Data were collected using purposive sampling technique. A total number of samples of the female reproductive system received in the department during the study period was 920 of which 309 samples of neoplastic lesions were included in the study. All the surgical specimens following mastectomy, trucut biopsy (breast), hysterectomy, oophorectomy and cervical biopsies were included in this study. All non- neoplastic surgical specimens of female genital tract and all specimens with inconclusive reports were excluded from the study. Clinical information and presentation of the tumors, age of the patients and site of the tumors were noted from the requisition forms. These specimens were fixed in 10% formalin. The gross examinations were done in histopathology department by a pathologist. Representative sections were taken and paraffin blocks were prepared. After cutting, the slides were stained with hematoxylin and eosin stain and mounted with distyrene plasticizer and xylene (DPX). After thorough microscopic examination a histopathological diagnosis was given. All the tumors were classified according to the World Health Organisation- Classification of tumors of female genital organs and breasts.[6] Data was entered and analysed by using Microsoft Excel.

RESULTS

A total of 309 samples of neoplastic lesions were studied over a period of five years. Total number of benign cases were 248 and 37 cases were malignant; the remaining being premalignant (cervix) and borderline/ intermediate (ovary) categories. Maximum number of women (112) with neoplastic lesions was in the age group of 41 to 50 years with all benign, malignant and premalignant also being common in the same age group of 41 to 50 years. The mean age of the women with neoplastic lesions was 41.64 with the standard deviation of 13.95.

Table 1. Distribution of Benign and Malignant Tumors by Age Groups (n = 309).

Age Group (Year)	Benign	Malignant	Others	Total
Up to 20	14(5.64)	0	1(4.16)	15(4.85)
21-30	53(21.37)	3(8.10)	2(8.33)	58(18.77)
31-40	49(19.75)	4(10.81)	9(37.5)	62(20.06)
41-50	90(36.29)	13(35.13)	9(37.5)	112(36.24)
51-60	24(9.67)	9(24.32)	2(8.33)	35(11.32)
61-70	7(2.82)	5(13.51)	0	12(3.88)
>70	11(4.43)	3(8.10)	1(4.16)	15(4.85)
Total	248(100)	37(100)	24(100)	309(100)

Youngest age of the patient showing neoplastic lesion was 12 years with diagnosis of fibroadenoma of the breast. Oldest age showing neoplastic lesion was 80 years with diagnosis of mature cystic teratoma, ovary.

Of the total neoplasms of female reproductive system, 32 (10.36%) were from uterine cervix, 124 (40.13%) were from uterine corpus, 105 (33.98%) were from ovary, 45 (14.56%) were from the breasts and 3(0.97%) were from vulva. Out of the benign neoplasms, majority were seen in the uterine corpus (47.18%) followed by ovary (38.71%), breasts (12.90%), vulva (0.81%) and uterine cervix (0.40%). Among the malignant neoplasms, maximum cases were seen in breasts (35.14%) followed by uterine cervix (32.43%), uterine corpus (16.22%), ovary (13.51%) and vulva (2.70%).

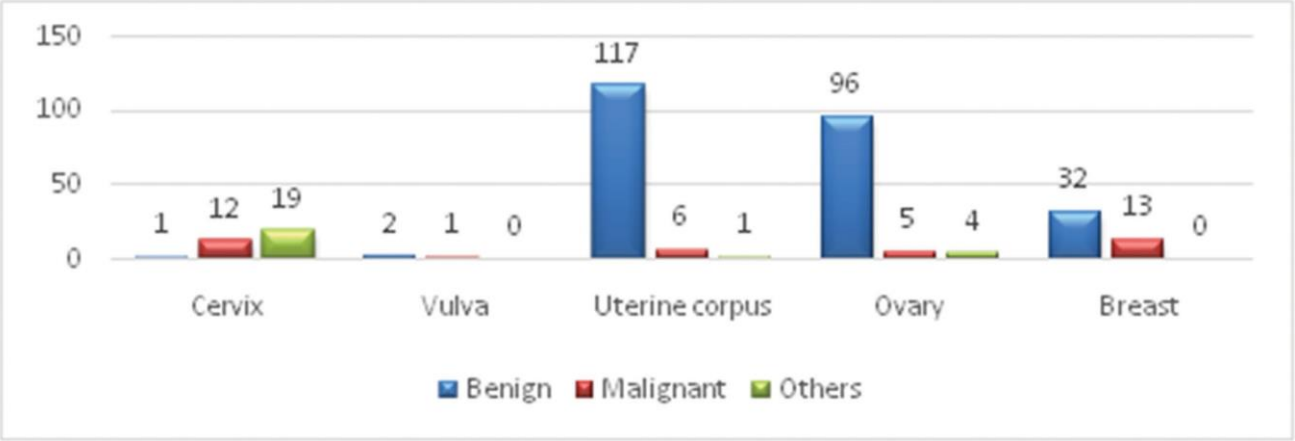

Figure 1. Distribution of neoplastic cases in various organs of female reproductive system.

Table 2. Histopathopathological spectrum of neoplasms in female genital tract.

Cervix	**Frequency (%)**
Benign	1(3.13)
Leiomyoma	1(3.13)
Malignant	12(37.5)
Squamous cell carcinoma	12(37.5)
Preneoplastic	19(59.39)
CIN-I	13(40.63)
CIN-II	3(9.38)
CIN-III	3(9.38)
Total	32(100)
Vulva	
Benign	2(66.67)
Fibroepithelial polyp	2(66.67)

Malignant	1(33.33)
Squamous cell carcinoma	1(33.33)
Total	3(100)
Uterine Corpus	
Benign	117(94.35)
Leiomyoma	117(94.35)
Malignant	6(4.84)
Endometrial carcinoma	5(4.03)
Leiomyosarcoma (Low grade)	1(0.81)
Pre-malignant	1(0.81)
Endometrial intraepithelial neoplasia	1(0.81)
Total	124(100)
Ovary	
Benign	96(91.43)
Serous cystadenoma	29(27.62)
Mucinous cystadenoma	8(7.62)
Mucinous cystadenoma with mature cystic teratoma	2(1.9)
Mature Cystic Teratoma	45(42.86)
Brenner tumors	1(0.95)
Granulosa cell tumor	1(0.95)
Mucinous cystadenoma with mature cystic teratoma	4(3.81)
Papillary Serous cystadenoma	1(0.95)
Serous cystadenofibroma	4(3.81)
Steroid cell tumor, NOS	1(0.95)
Malignant	5(4.76)
Serous papillary cystadenocarcinoma	3(2.86)
Papillary mucinous cystadenocarcinoma	1(0.95)
Serous high grade carcinoma	1(0.95)
Borderline	3(2.86)
Papillary mucinous cystadenoma	2(1.9)

Serous borderline tumor	1(0.95)
Intermediate	1(0.95)
Sertoli Leydig cell tumor	1(0.95)
Total	105(100)
Breast	
Benign	32(71.11)
Fibroadenoma	29(64.44)
Benign Phylloides tumor	1(2.22)
Lactating adenoma	1(2.22)
Intraductal papilloma	1(2.22)
Malignant	13(28.89)
Invasive carcinoma, NOS	10(22.22)
Invasive micropapillary Carcinoma	1(2.22)
Mixed invasive lobular carcinoma with invasive ca, NST	1(2.22)
Mixed classic lobular carcinoma with pleomorphic variant	1(2.22)
Total	45(100)

Among the neoplastic lesions in the uterine cervix, commonest was the premalignant lesion (CIN) comprising 59.38% of the total cases followed by squamous cell carcinoma in 37.50%. The remaining one case was benign-cervical leiomyoma. In the vulva, only 3 cases of neoplastic lesions were identified two of which were fibroepithelial polyp (benign lesion) and one was squamous cell carcinoma (malignant lesion).

In the uterine corpus, commonest neoplastic lesion was benign (leiomyoma) accounting for 94.35% of the total cases in the uterine corpus. 6 cases (4.84%) of malignant lesions were found of which 5 were that of endometrial carcinoma and the remaining 1 was leiomyosarcoma.
1 case (0.81%) of premalignant lesion (endometrial intraepithelial lesion) was also found.

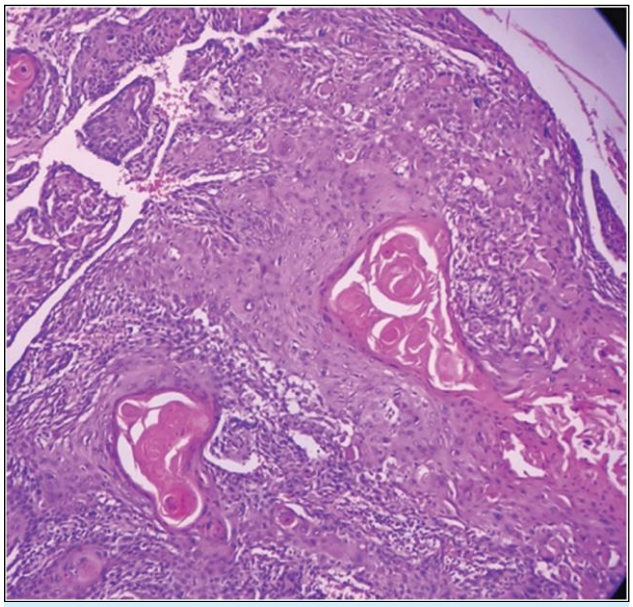

Figure 2. Squamous cell carcinoma, cervix, H and E, 100X.

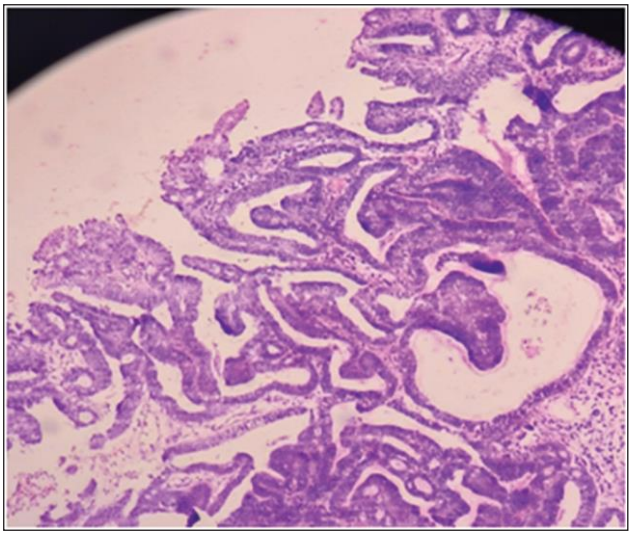

Figure 3. Endometrial carcinoma, H and E, 40X.

In the ovary, 91.43% (96 cases) were benign of which mature cystic teratoma was the commonest (45 cases). Serous cystadenoma accounted for 29 cases followed by mucinous cystadenoma (8 cases).6 cases of mucinous cystadenoma with mature cystic teratoma, 4 cases of serous cystadenofibroma and 1 case each of papillary serous cystadenoma , Brenner tumor, granulosa cell tumor, and steroid cell tumor, NOS was found. Malignant lesions accounted for 4.76% (5 cases) of the neoplastic lesions in the ovary of which serous papillary cystadenocarcinoma was the commonest (3 cases). 1 case each of high grade serous carcinoma and papillary mucinous cystadenocarcinoma were known. While, 3 borderline neoplastic lesions (2 cases of papillary mucinous cystadenoma and 1 case of serous borderline tumor) and 1 intermediate lesion (Sertoli Leydig cell tumor) were also identified. Among the neoplastic lesions of the breasts, 71.11% (32 cases) were benign lesions with majority of the cases being fibroadenoma. The remaining 28.89% were malignant lesions of which the commonest (10 cases) was invasive carcinoma, NOS. 1 case each of invasive micropapillary carcinoma, mixed lobular carcinoma with invasive carcinoma, NOS and mixed classic lobular carcinoma with pleomorphic variant were also identified.

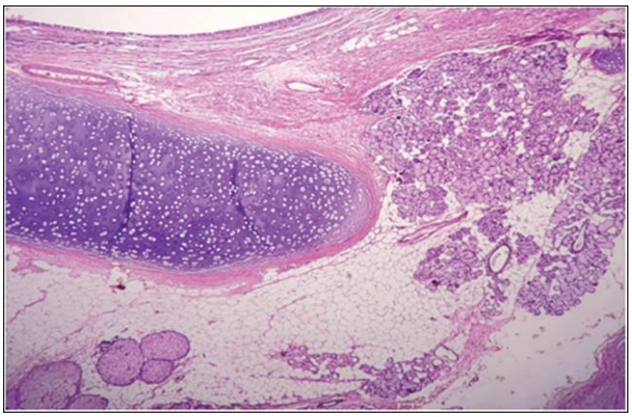

Figure 4. Mature cystic teratoma,ovary, H and E,100X.

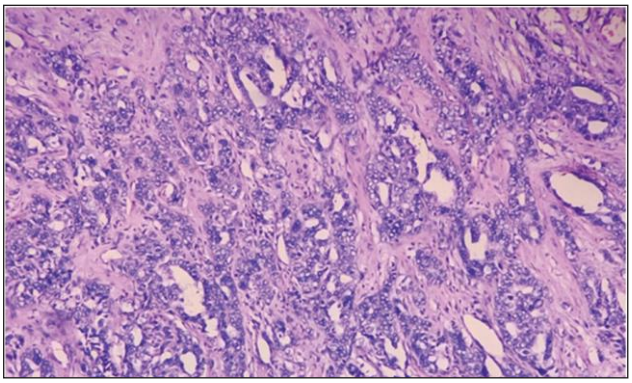

Figure 5. Invasive breast carcinoma NST,H and E,100X.

Table 3. Distribution of neoplastic lesions according to the laterality.

Table 3.1. Distribution of neoplastic lesions in Ovary according to the laterality (n = 105).

Distribution of Cases by Diagnosis	Right	Left	B/L	Total n=105
	n (%)	n (%)	n (%)	n (%)
Benign	49 (90.74)	41(95.35)	5(62.5)	95(90.48)
Borderline	0	1(2.33)	2(25)	3(2.86)
Intermediate	1(1.85)	0	0	1(0.95)
Malignant	4(7.41)	1(2.33)	1(12.5)	6(5.71)

This data shows both benign and malignant neoplastic lesions of the ovary were common in the right ovary (49 cases of benign neoplasms and 4 cases of malignant neoplasms).

Table 3.2. Distribution of neoplastic lesions in Breast according to the laterality (n = 45).

Distribution of Cases by Diagnosis	Right	Left	B/L	Total n =105
	n (%)	n (%)	n (%)	n (%)
Benign	15(60)	11(78.57)	6(100)	32(71.11)
Malignant	10(40)	3(21.43)	0	13(28.89)

In the breast, among 45 neoplastic cases, both benign and malignant neoplasms were more common in the right breast (15 benign and 10 malignant) than the left (11 benign and 3 malignant). The remaining cases were seen in bilateral breasts (6 cases).

DISCUSSION

Female reproductive system includes ovaries, fallopian tubes, uterine corpus and cervix, vagina, vulva and breasts. Breasts, uterine corpus, cervix and ovaries are the common sites of occurrence of neoplastic lesions. Vulvar, vaginal, fallopian tube cancers, and choriocarcinomas are very rare. There is a marked variation in the distribution of cancers according to the sites in different geographic regions. The incidence rate of female breast cancer in some developed regions (Australia, New Zealand, North America) is nearly three times higher than that in developing regions (South-central Asia, Middle Africa, East Africa).[7]

Neoplasms of vulva and vagina:

Carcinoma of the vulva accounts for 4% of all female genital cancers and occurs mainly in women aged over 60 years. Squamous cell carcinoma is the most common type (86%). These tumors are divided into two groups: keratinizing squamous cell carcinomas unrelated to HPV (> 70% of cases), and warty and basaloid carcinomas, which are strongly associated with high-risk HPV (< 25% of cases), mainly HPV16. Primary malignant tumors of the vagina are uncommon, constituting about 2% of all genital tract tumors. Most (80%) vaginal malignancies represent metastatic spread. Squamous cell carcinomas account for over 90% of primary vaginal malignancies.[8] In our study, we had 1 case of squamous cell carcinoma of the vulva in a 55 years old lady. This finding is similar to the observation made by Mohammad A et al and Kumar N et al where 1 case of vulval malignancy was reported.[2,4]

Neoplasms of cervix:

Cervical cancer remains the fourth most common cancer in women worldwide. About 90% of the new cases and deaths worldwide in 2020 occurred in low- and middle-income countries. More than 95% of the cases of cervical cancer is attributed to Human Papilloma virus (HPV) and women living with HIV are 6 times more prone to develop the disease in comparison to healthy women.[9] Pap smear examination as a screening tool and availability of HPV vaccines as a preventable measure have contributed by large to reduce the incidence and mortality of cervical carcinoma in many countries. 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.[2] But lack of awareness among the

people, high cost of the vaccine and reluctance to seek timely health care still make these tools inaccessible to the people in Nepal and thus may still account for the common malignancy in women in our part of the world.[5,10] In this study, 32.43% of the total malignant neoplasms were seen in the cervix, which reflects the high burden of cervical cancer in our part of the world. However, this study also has revealed that cervical cancer can be detected in preinvasive state (CIN) with the use of adequate screening methods so that adequate measures can be taken to prevent its progression to invasive cancer. 19 cases of premalignant lesions were detected in this study with majority of them being CIN I. Cervical carcinoma is also the commonest malignant neoplasm in the studies by Singh M et al and Pokharel HP et al comprising 55..55% and 67.3% respectively of the total malignant neoplasms of female genital tract.[5,13]

Neoplasms of uterine corpus:

In the current study, neoplastic lesions of the female reproductive tract were most commonly seen in the uterine corpus (40.13% of the total cases). This finding is in accordance with the study conducted by Mohammad A and Makaju R where neoplastic lesions of the uterine corpus occupied 33.35% of the total cases and also in a study by Paul et al occupying 64% of the total cases. [2,11] The commonest benign neoplasm among all was leiomyoma (37.86 % of the total neoplasms) in this study which is similar to the findings by Kumar N et al and Singh M et al.[4,5] The commonest risk factor for development of fibroid is age of the patient. This tumor was seen more commonly in 5th and 6th decade than 3rd decade of life.[8,9] It has been studied that over 70% of the female by the time of onset of their menopause may present with uterine fibroid.[10,11,12] In this study, leiomyoma was most commonly seen in 4th decade of life similar to that by Kumar N.[4] All the cases of leiomyoma were seen in the uterine corpus except one which was seen in the uterine cervix. Also, 5 cases of endometrial carcinoma were detected that accounted for 13.5% of malignant neoplasms of female genital tract making it the third commonest female genital tract malignancy in this study along with the ovarian cancers. This finding is similar to that of Khaniya et al and Pokhrel et al.[12,13] The low incidence of endometrial cancer may be due to the low incidence of obesity, hypertension, diabetes mellitus in our country as compared to the west.[12]

Neoplasms of Ovary:

Ovarian cancer accounts for 15-25% of all gynaecological malignancies, yet it is responsible for approximately 50% of the deaths from cancer of female genital tract. Ovarian neoplasms are not associated with significant symptoms and most women present with advanced disease. [14] In this study, 91.43% of ovarian neoplasms were benign with mature cystic teratoma being the commonest. 5 cases of malignant neoplasms were seen with serous cystadenocarcinoma being the commonest. In a study by Garg et al between 2013 to 2016 entitled "Study of histomorphological spectrum of ovarian tumors" and another study by Mondal et al, the commonest benign ovarian tumor was serous cystadenoma followed by mucinous cystadenoma and mature cystic teratoma.[15,16] In this study, benign ovarian neoplasms were seen most commonly in the age group of 21 to 30 years (35.2%). However malignant lesions were seen in a wide age group of 20 to 60 years. This finding is different from that by Vaidya S et al where benign neoplasms of the ovary was common in 3rd and 4th decades of life and malignant tumors were seen after 4th decade.[14]

Neoplasms of Breast:

Breast cancer is the most frequently diagnosed cancer in women worldwide. Incidence rates are

higher in North America, Australia and Europe and less common in African and Asian countries. Factors associated with this international variation in incidence include those related to early detection, particularly the availability of mammography screening, as well as the prevalence of established risk factors, including overweight/obesity, use of menopausal hormone therapy, physical inactivity, and alcohol consumption.[17] The incidence of breast cancer is increasing in the developing world due to increased life expectancy, urbanization and adoption of western lifestyles. Breast cancer is the second most common malignancy among Nepalese women. [18] This is also supported by our study where infiltrating ductal carcinoma of the breast is the commonest malignant neoplasm, occupying 35.15% of the total malignant neoplasms in females which is followed by squamous cell carcinoma of the cervix. Breast carcinoma was the commonest malignancy in the study by Kumar N et al attributing to 43.42% of the neoplastic cases was the second common malignancy in the study by Singh M et al accounting for 33.33% of the total malignant cases.[4,5] Maximum number of breast carcinoma was seen in the age group of 40 to 50 years which is similar to that of various population based studies performed in different parts of Nepal.[18] The commonest benign neoplasm of the breast is fibroadenoma occupying 9.38% of the neoplasms of female reproductive system which is similar to the finding by Singh M et al.[5]

CONCLUSIONS

Current study shows uterine corpus to be the commonest site of malignancy of the female reproductive system with leiomyoma being the commonest benign neoplasm. The commonest malignancy is infiltrating ductal carcinoma of the breast followed by squamous cell carcinoma of the cervix. Since malignant neoplasm of the female reproductive system contributes to the major cancer burden in the world, special emphasis should be given to reduce its incidence. Pap screening and HPV vaccination should be made accessible to all, especially the high risk group to reduce cervical cancer. Likewise, the role of self-breast examination and mammography is crucial to reduce the burden of breast cancers.

Limitation: This is the hospital based study and thus it doesn't represent the entire population. Similarly, missing data from hospital records might have affected the sampling.

ACKNOWLEDGEMENTS

I would like to express my sincere gratitude to all the coauthors of this paper and the faculties, residents, technical and non-technical staffs at Department of Pathology, College of Medical Sciences, my family and above all, the patients without whom this research paper would not have been possible.

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Citation: Sedhain M, Pathak P, Goyal B, Subedi P. Histopathological Spectrum of Neoplastic Lesions of Female Reproductive System at a Tertiary Care Hospital in Bharatpur, Chitwan. JCMS Nepal. 2023; 19(1); 15-25.