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Incidence of neoplastic lesions of female genital tract in a tertiary care centre: A 3 year retrospective study

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Abstract

Aims & objectives

1. To determine the frequency distribution of the benign and malignant tumors occurring in female genital tract.
2. To find out the age distribution of occurrence of benign and malignant tumors in female genital tract.
3. To find out the incidence of malignancy in female genital tract in a local population.

Materials and Methods: This study was carried out on the rural population in a tertiary care centre on 520 cases where the data and histopathology slides were retrieved from the hospital records from September 2016 to August 2019.

Results: A total of 520 FGT surgical biopsies with various types of neoplastic lesions were received. Out of which 375 were non-neoplastic and 145 were neoplastic lesions. Among the 145 neoplastic cases, 113 cases (77.93%) were reported as benign, 16 cases (11.03%) premalignant and 16 cases (11.03%) were malignant. Leiomyoma was the most common benign tumor of uterine body and squamous cell carcinoma of cervix was the most common malignant tumor. Both benign and malignant tumors were reported in the age group of 41-50 years and 31-40 years respectively.

Conclusion: Leiomyoma is the commonest benign tumor arising in the female genital tract. Squamous cell carcinoma of cervix is the common malignant tumor. Routine screening tests are mandatory for reducing the incidence of malignancies and pre-malignant lesions of the female genital tract especially in high risk patients.

Keywords: Female genital tract (FGT), leiomyoma, malignant neoplastic, squamous cell carcinoma

Introduction

The female genital tract includes vulva, vagina, uterus (body & cervix), fallopian tubes, and ovaries. The common sites for the development of the neoplastic lesions are cervix, endometrium, myometrium and ovaries. According to Worldwide cancer data 2018, breast cancer was the most common cancer in women worldwide, contributing 25.4% of the total number of new cases and cervical cancer was the fourth most common cancer in women, contributing 6.9% of the total number of new cases ^[1].

In female genital tract, endometrium is hormone sensitive which constantly undergoes changes in the reproductive life. Endometrial polyp is one of the common causes of Abnormal Uterine Bleeding (AUB) in the reproductive age group as well as postmenopausal age group. Endometrial polyp is a focal hyperplastic growth of endometrial glands and stroma and is benign lesion commonly, which can rarely become malignant ^[2]. Endometrial Carcinoma (EC) is commonest between the ages of 65 to 85 years but can also arise early even before the age of 45 years in up to 5% ^[3].

Histological examination by colposcopy guided biopsies is still considered the “gold standard” in the assessment of cervical lesions; however, the histologic assessment of these lesions is limited to the interpretation of the morphology, with little to no information regarding the risk of persistence, progression, or regression ^[4]. In addition, histologic assessment of cervical lesions is complicated by inter-observer variability ^[4].

In ovaries, the most common ovarian lesions include benign non neoplastic lesions and neoplastic lesions including functional cysts and ovarian tumors respectively. Ovarian lesions affect all age groups ^[5]. The clinical course of different histologic types of ovarian

tumors are much variable [6, 7]. Most ovarian cancers are detected when they have spread beyond the ovary [8]. So they have the worst prognosis and highest case fatality rate among all gynaecological malignancies [9, 10].

Present study focuses on neoplastic lesions of endometrium, cervix and ovary in the population of the tertiary care centre.

Material and methods

The study was conducted after the approval from the Institutional ethical committee and consent was taken from all the patients. All the uterine cervical biopsies, endometrial curettings and hysterectomy specimens received in Department of Pathology over a period of 3 years i.e. from September 2016 to August 2019 were included in the study. A total of 520 specimens were included and slides were retrieved from the archives of the Department of Pathology. Wherever necessary new sections were made from the formalin fixed paraffin embedded blocks and stained with Haematoxylin and Eosin. The data was analysed using SPSS version 16. The data was represented as frequency and percentage of the numbers.

Inclusion criteria

1. Patient belonging to age group 21-80 years.
2. Various neoplastic lesions of female genital tract are included in the study.

Exclusion criteria

1. Non neoplastic lesions of female genital tract.
2. Specimens of the breast.

Observations

A total of 520 cases were recorded and the age ranged from 21-80 yrs with a mean age of 45.16 ±9.3 years. The youngest patient in the study was 21 years and the oldest was 80 years of age.

Among 520 specimens, total hysterectomy specimens were found to be 103, endometrial curettings-156, cervical biopsies-37. Total number of salpingectomy, oophorectomy and salpingo oophorectomy specimens were 7, 3 and 3 respectively. There were only two specimens of vulval biopsy and single specimen of vaginal vault and vulval cyst respectively. Among polyps, cervical polyps were 14 in number and endometrial polyp were 10 in number.

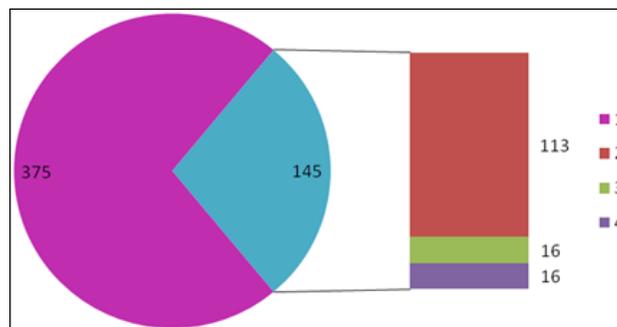


Fig 1: Frequency of lesions in female genital tract

Fig 1: Shows out of 520 specimens, 375 cases (72.11%) were non neoplastic and 145 cases (27.89%) were neoplastic. Among the 145 neoplastic cases, 113 cases (77.93%) were reported as benign, 16 cases (11.03%) premalignant and 16 cases (11.03%) were malignant

Table 1: Frequency of lesions according to site (neoplastic and non-neoplastic lesions)

Neoplastic		Cervix	Ovary	Endometrium & myometrium	Fallopian tube	Vulva
	Benign	30(20.6%)	08(5.51%)	75(51.7%)	-	-
	Premalignant	06(4.13%)	-	10(6.89%)	-	-
	Malignant	08(5.51%)	01(0.68%)	07(4.82%)	-	-
Non-neoplastic		54(14.4%)	74(19.7%)	219(58.4%)	25(6.6%)	3(0.8%)

Table 1: Shows frequency distribution of total number of lesions according to the site with maximum number of cases of lesions reported in endometrium (59.80%), followed by

cervical lesions (18.85%), ovary (15.96%), fallopian tube (6.6%) and vulva (0.8%).

Table 2(a): Lesions according to histopathological diagnosis (non neoplastic lesions)

Cervix	Ovary	Endometrium & myometrium	fallopian tube	Vulva
Chronic cervicitis 23(6.13%)	Unremarkable 20(5.33%)	Proliferative phase 69(18.4%)	Unremarkable 20(5.33%)	Keratinized Stratified squamous epithelium 02(0.53%)
Papillary endocervicitis 12(3.2%)	Corpus albicans 23(6.13%)	Disordered proliferative phase 17 (4.53%)	Hydrosalpinx 03(0.8%)	Mucous cyst 01(0.26%)
Nabothian cyst 19(5.06%)	Corpus luteum 29(7.73%)	Secretory phase 77(20.53%)	Partubal cyst 01(0.26%)	
	Endometriosis 01(0.26%)	Atrophic 19(5.06%)	Xanthogranulomatous salpingo-oophoritis 01(0.26%)	
	Xanthogranulomatous salpingo- oophoritis 01(0.26%)	Hormonal effect 13(3.46%) Adenomyosis 17(4.53%) Endometritis 07(1.86%)		

Table 2(b): Lesions according to histopathological diagnosis (neoplastic lesions)

	Benign	Premalignant	Malignant
Cervix	Squamous metaplasia 13 (8.96%)	Cervical dysplasia 06(4.13%)	Squamous cell carcinoma 07(4.82%)
	Endocervical polyp 14(9.65%)		Small cell carcinoma 01(0.68%)
	Leiomyoma 03 (2.06%)		
Ovary	Serous cystadenoma 05(3.44%)	-	Mucinous cystadenocarcinoma 01(0.68%)
	Brenner tumor 01(0.68%)		
	Teratoma 02(1.37%)		
Endometrium & myometrium	Leiomyoma 65(44.82%)	Typical hyperplasia 10(6.89%)	Adenocarcinoma 07(4.82%)
	Endometrial polyp 10(6.89%)		

Table 2(a & b)

According to histopathological diagnosis in non-neoplastic lesions, the most common diagnosis in cervical biopsies was chronic nonspecific cervicitis (6.13%) followed by nabothian cyst (5.06%) papillary endocervicitis (3.2%). In the endometrium, majority of the cases were reported as secretory phase (20.53%) and proliferative endometrium (18.40%). The other histopathological diagnosis were disordered proliferative phase, atrophic, hormonal effect and endometritis.

In the ovary, apart from corpus luteum (7.73%) and corpus albicans (6.13%), the other lesions reported were endometriosis (0.26%) and xanthogranulomatous salpingo-oophoritis (0.26%).

Fallopian tube and vulva were unremarkable in majority of the cases.

Among the neoplastic lesions of the cervix, endocervical polyp was the most common benign lesion (9.65%), with squamous intraepithelial lesion comprising 4.13% cases and total of 5.50% of malignant lesions out of which 4.82% were squamous cell carcinoma on morphology (4 cases of keratinizing and 3 non-keratinising) and (0.68%) small cell carcinoma.

In the endomyometrium, leiomyoma (44.82%) was the most common benign tumor, 6.89% were reported as benign/typical hyperplasia and 4.82% cases of malignant tumors (4 cases of endometrioid adenocarcinoma and 3 papillary serous carcinomas).

In the ovary, the benign tumors reported were benign serous cystadenoma (3.44%), brenners tumor (0.68%) and teratoma (1.37%). Only one malignant case (0.68%) was reported- mucinous cystadenocarcinoma.

Table 3: Age distribution of neoplastic lesions

Age (yrs)	Cervix			Endometrium			Ovary		
	Benign	pre malignant	malignant	benign	pre -malignant	malignant	Benign	pre malignant	malignant
21-30	02 (1.32%)	-	-	04 (2.75%)	-	-	01 (1.68%)	-	-
31-40	08 (5.51%)	-	03 (2.06%)	23 (15.86%)	03 (2.06%)	01 (0.68%)	-	-	-
41-50	11 (7.58%)	02 (1.37%)	03 (2.06%)	32 (22.06%)	05 (3.44%)	-	03 (2.06%)	-	-
51-60	07 (4.82%)	03 (2.06%)	01 (0.68%)	09 (6.20%)	-	02 (1.32%)	02 (1.32%)	-	-
61-70	02 (1.37%)	01 (0.68%)	01 (0.68%)	05 (3.44%)	02 (1.37%)	04 (2.75%)	-	-	01 (1.68%)
71-80	-	-	-	02 (1.37%)	-	-	02 (1.32%)	-	-

Table 3: Shows maximum number of benign lesions reported as leiomyomas (22.06%) were found in the age group of 41-50 years. Among the malignant lesions, carcinoma cervix was reported age group of 31-40years (2.06%) and 41-50 years (2.06%) where as in endometrium, maximum number of malignant lesions (2.75%) were found in age group of 61-70 years. One case of mucinous cystadenocarcinoma in the ovary was found in the age group of 61-70 years

Discussion

Neoplasms of the female reproductive system-namely cancer of the cervix uteri, cancer of the corpus uteri and ovarian cancers are important cause of cancer morbidity and mortality worldwide [11].

In the present study conducted in a tertiary care centre in the rural set up, a total of 520 surgical specimens of female genital tract were received of which 145(27.88%) were found to be neoplastic which is similar to a study done by Gaikwad SL *et al* (29.78%) [12].

Among the total neoplastic lesions in the present study, 77.93% were benign lesions. Similarly in a study done by Paul S N *et al*. [13], 90% lesions were reported as benign lesions among the total neoplastic lesions which is higher compared to our study. In the present study, benign lesions of cervix reported were endocervical polyp (9.65%) followed by squamous metaplasia and cervical leiomyoma with majority of the cases in 31-40 and 41-50 years of age. Gaikwad SL *et al*. [12] reported 4.68% of cervical polyps in the age group of 31-40 years. In our study, benign lesions of

endometrium and myometrium were endometrial polyp and leiomyoma. Among these, uterine leiomyoma was the commonest lesion accounting for 44.82% out of total neoplastic lesions, most common in 31-50 years age groups. Gaikwad SL *et al.* [12] also reported leiomyoma (57.85%) as the most common benign tumor among all the neoplastic lesions with maximum incidence in 31-50 years of age. Mangala Gowri *et al.* also noted similar results in their study [14]. Among the ovarian lesions, serous cystadenoma was the commonest benign neoplasm of ovary (3.44%) among the neoplastic lesions with maximum incidence in the age group of 71-80 years. Other benign lesions were Brenner tumor 0.68% and mature cystic teratoma 1.37% with both in age group of 41-50 years. Studies done by Paul SN *et al.* [13] and Gaikwad SL *et al.* [12], reported high incidence of serous cystadenoma compared to our study i.e. 6% and 9.28% with maximum in the age group of 41-50 and 31-40 years respectively.

The pattern of gynecological malignancies varies with age, ethnicity, regional differences, family history, parity, usage of oral contraceptive pills and hormone replacement

therapy. In our study, majority of malignant lesions were found in cervix in which most common histological type was squamous cell carcinoma (4.82%) out of the total neoplastic lesions. All these carcinomas were reported on cervical biopsies in the age group of 31-40 and 41-50 years. Similar observations were also noted in the study by Khandekar S *et al.* (6.28%) [15] while other studies by Gaikwad SL *et al.* [12], Singh M *et al.* [16] and Paul SN *et al.* [13] reported squamous cell carcinoma as 9.28%, 7.04% and 7% respectively. In our study, the other histological variant of cervical carcinoma reported was a single case of small cell carcinoma in the age group of 41-50 years. Similarly, Dhakal HP *et al.* [17] also noted various other less common histological types of cervical carcinomas out of all the cervical cancers (1293 cases) in their study namely adenocarcinoma (3.8%), small cell carcinoma (0.3%), adenosquamous carcinoma (0.2%) and carcinosarcoma (0.2%) whereas in a study by Rahman MA *et al.* [18], cervical adenocarcinoma (1.08%) out of 62 cases of gynecological cancers, was also found other than squamous cell carcinoma.

Table 4: Comparison of the incidence of malignancies of the female genital tract reported in various studies

Sites	Present Study	Gaikwad SL [12]	Khandekar S [15]	Singh M <i>et al</i> [16]	Paul S N <i>et al</i> [13]
Cervix (squamous cell carcinoma)	5.51%	9.28%	6.28%	7.04%	7%
Endometrium (adenocarcinoma)	4.82%	2.14%	3.38%	-	-
Ovary (mucinous cystadenocarcinoma)	0.68%	0.71%	0.96%	-	-

The incidence of cervical cancer is declining in the last three or four decades in most developed countries predominantly due to effective population based cervical screening programs, treatment of pre-invasive condition, decreased parity and better living condition [19]. Low rates are also observed in China, Western Asia and most of the Muslim countries, including Pakistan, Iran and Saudi Arabia [20-24]. In a study on gynecological cancer profile less cigarette smoking in females, religious practices and male circumcision was thought to be some of the possible reasons for the low incidence of cervical cancer [22].

Out of total neoplastic lesions, the premalignant lesions of cervix were found to be 4.13%. These cases showed cervical dysplasia with three cases of LSIL and HSIL each. Specialized investigations (Elisa, HPV serology and immunohistochemistry) could not be carried out in our set up due to non-availability and high cost incurred. The effectiveness of Pap test in detecting cervical precancers, easy accessibility to cervix by colposcopy and biopsy are the best tools for early detection and eradication of pre-invasive lesions, some of it may progress to cancer if not diagnosed and treated timely [13]. This could be the reason that 80% of the cancers occurring in women of developing countries comprise of cervical cancer and it accounts for the fourth common cause of mortality among all cancers [25].

In our study majority of the women with endometrial cancer were in the age group of 61-70 years similar to the study of Gaikwad SL *et al.* [12] who also reported incidence of endometrial carcinoma in 6th and 7th decade. The mean age of endometrial cancer ranged from 52 to 57 in other studies [17, 26]. The percentage of carcinoma endometrium in our study constituted 4.82% cases of the total neoplastic lesions. In the study conducted by Gaikwad SL *et al.* [12] and Khandekar S *et al.* [15] only 2.14% and 3.38% of endometrial

carcinomas respectively, were reported which is lower as compared to our study. Endometrioid adenocarcinoma was reported to be the most common malignant tumor which is comparable with the other studies also [17, 18, 26]. In our study, out of 7 endometrial carcinomas, 4 were high grade and 3 were low grade according to FIGO grading system. This low incidence of endometrial cancer could be due to the low incidence of obesity, hypertension, diabetes mellitus, breast cancer and family history of breast/ovarian cancer in our context compared to the West [27]. Also various studies showed that incidence of this malignancy is higher in the more developed countries and lower in Asia and Africa [19, 22, 28, 29].

In our study, premalignant lesions of endometrium were found to be 10 cases (10.86%) out of total neoplastic lesions of endometrium (classified according to the 2014 WHO classification of endometrial hyperplasia). The findings of our study are similar to study done by Vaidya S *et al.* (10.42%) [30] where as in a study conducted by Baral R *et al.* [31] the percentage of precursor lesions was reported 18.30% which is slightly higher than our study. In our study all the cases were in the category of hyperplasia without atypia. Similar results were seen in the study by Nanda J *et al.* [32]. Endometrial cancer is histologically diverse group of neoplasms characterized by a different pathogenesis. Estrogen-dependent tumors (type I) are low grade and frequently associated with endometrial hyperplasia, in particular atypical hyperplasia [33]. Unopposed estrogenic stimulation is the driving force behind this group of tumors. [33] It may be the result of anovulatory cycles that occur in young women with the polycystic ovary syndrome or due to normally occurring anovulatory cycles at the time of menopause. The iatrogenic use of unopposed estrogens as hormone replacement therapy in older women also is a

predisposing factor for the development of endometrial cancer [33]. According to WHO, the second type (type II) of endometrial cancer appears less related to sustained estrogen stimulation [33].

In 20% of endometrial hyperplasia and 50% of endometrioid cancers, PTEN suffers a loss-of-function mutation or a null mutation, making it less effective or completely ineffective [34]. Loss of PTEN function leads to up-regulation of the PI3k/Akt/mTOR pathway, which causes cell growth [35]. When a mutant version of p53 is overexpressed, the cancer tends to be particularly aggressive [34]. Type I and Type II cancers tend to have different mutations involved. ARID1A, which often carries a point mutation in Type I endometrial cancer, is also mutated in 26% of clear cell carcinomas of the endometrium, and 18% of serous carcinomas. Epigenetic silencing and point mutations of several genes are commonly found in Type I endometrial cancer [36, 37]. Mutations in tumor suppressor genes are common in Type II endometrial cancer [36]. PIK3CA is commonly mutated in both Type I and Type II cancers [37]. In women with Lynch syndrome-associated endometrial cancer, microsatellite instability is common [35].

Ovarian cancer has worst prognosis of all cancers of female reproductive organs, however, some studies have reported that use of oral contraceptive pills reduces its incidence [38]. Present study showed only a single malignant tumor of ovary i.e. mucinous cystadenocarcinoma accounting for 0.68% out of total neoplastic lesions. This study is similar to the study by Gaikwad SL *et al.* [12] where it was reported as 0.71% as compared to 0.96% reported in a study by Khandekar S *et al.* [15].

The increased risk of ovarian cancer particularly of surface epithelial tumors (SETs) is associated with use of hormone replacement therapy (HRT) [39] tobacco consumption [40] family history of ovarian cancer and breast cancer [41] and mutation of BRCA1 and/or BRCA2 [40].

Among all the gynecological cancers, ovarian tumors represent the greatest challenge to clinicians and the pathologists because it is very difficult to diagnose it in early stage due to its nonspecific symptoms and asymptomatic nature in many cases. Therefore the clinical symptoms, radiological findings, and other ancillary investigations such as CA-125, CA-19-9 and CEA play a role in the early preoperative diagnosis of ovarian carcinoma.

Conclusion

In this study, squamous cell carcinoma was the most frequent malignant tumor of the cervix whereas uterine leiomyoma was the commonest among the benign lesions of female genital tract in the age group of 31-50 years. There is the need to increase awareness and counsel the rural population regarding the risk factors and screening programs available for the malignancies of the female genital tract to reduce morbidity and mortality.

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