Histopathological Analysis of Various Lesions of the Female Genital Tract in the Reproductive and Post Reproductive Age Group in a Tertiary Care Centre

Bipi Das¹, Saumendra Bhattacharjee², Jyotimala Gogoi³

ABSTRACT

Introduction: Cancer of female genital tract are important causes of morbidity and mortality worldwide. Incidence and pattern of various cancers in female genital tract is important to know the nature and extent of cancer in a particular region. The aims and objectives of this study were to study the histopathological pattern and age-wise distribution of various lesions.

Material and methods: A total of 471 cases were studied retrospectively from January 2019 to December 2019. They were reviewed and analysed for age and histopathological findings.

Results: Out of the total 471 cases, 419(89.15%) cases showed benign and 52 (11.06%) cases presented with malignant lesions. Most common benign lesion in ovary was mucinous cystadenoma (55.55%) (20-60 years) whereas most common malignant lesion was serous cystadenocarcinoma (60%) (20-40 years). In the uterus proliferative endometrial lesion was present in 35.23% cases (30-60 years) while leiomyoma was seen in (56.14%) cases in 30-40 years age group. 96 cases (77.5%) in age group 30-60 years presented with chronic non specific cervicitis while malignant- squamous cell carcinoma of cervix was seen in 16% cases (30-50 years).

Conclusion: The histopathological examination revealed that most lesions in the reproductive age group (15-45 years), were benign. But malignant lesions were most common in the post reproductive age group (i.e., above 46 years).

Keywords: Reproductive and Nonreproductive Age Group, Benign, Malignant

INTRODUCTION

The female reproductive organ can be divided into the upper genital tract (i.e., uterus, fallopian tube, ovaries and cervix), the lower genital tract (i.e., vulva and vagina). Female genital tract lesions are commonly seen in ovary, uterus (body/cervix), vagina, less commonly in fallopian tube and vulva. Around menopause, changes in the genital organs occur rapidly. Menstrual cycle stops and the ovaries stop producing oestrogen. After menopause the tissues of the labia minora surrounding the opening of clitoris, vagina and urethra undergo atrophy. Vaginal infections are more likely to develop and size of uterus, fallopian tubes and ovaries decrease. With ageing, there is decrease in the amount of connective tissue, muscles, ligaments that support the uterus, vagina and rectum. As a result there is increase in the susceptibility of prolapse. The cancer of the female genital tract such as carcinoma cervix, endometrium and ovary are important causes of morbidity and mortality worldwide.¹ Carcinoma cervix is the 2nd most common cancer in women and 8th most common cancer overall. In India cervical cancer contributes to approximately 6-29% of all cancers in women. Women are most of the time unaware of the signs and symptoms associated with these tumours so that these malignancies are also referred to as silent killers. Among all gynaecological malignancies, carcinoma ovary ranks 3rd most common cancer in India² and it contributes to about 5.9% of total cancers among women in India.² It has the highest mortality rate as it is detected in advanced stage in 2/3rd cases. No reliable screening test is available for early detection of ovarian tumours. These tumours are also difficult to distinguish based on their clinical, radiological and gross picture, so it is important to do histopathological examination to know the true nature of these tumours. In advanced nations the leading forms of malignancies in the female genital tract are of the ovary and endometrium. While in the middle and low socio – economic countries carcinoma cervix is most common.¹ On global basis the cancer of FGT rank as:-

Ca cervix – 2nd most common
Ca ovary – 7th most common
Ca body of the uterus – 8th most common

This study was done to find out the occurrence of various histopathological types of lesions of female genital tract at pre-menopausal and post menopausal age group.

MATERIAL AND METHODS

This was a 1 year retrospective study done at the department of Pathology, Silchar Medical College and Hospital, India, for the period of January 2019 to December 2019. Various specimens were obtained by hysterectomy, biopsies from

¹Post Graduate Trainee, Department of Pathology, Silchar Medical College and Hospital, ²Demonstrator, Department of Pathology, Silchar Medical College and Hospital, ³Post Graduate Trainee, Department of Pathology, Assam Medical College and Hospital, India

Corresponding author: Dr. Bipi Das, Post Graduate Trainee, Department of Pathology, Silchar Medical College and Hospital, India

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cervix, endometrium and from external genitalia were fixed in 10% formalin (available as 40% formaldehyde) for 24 hours at room temperature. Gross examination was done. Sections of 3-5mm thickness were taken from the representative areas. Tissues were then processed by the following steps:
1. Dehydration done by passing the tissues through series of progressively concentrated alcohol (isopropylalcohol) baths.
2. Clearing done by xylene.
3. Impregnation in wax which removed the clearing agent.
4. Embedding done by placing the tissues in a mould filled with paraffin wax held at 2-4°C above its melting point.
5. Paraffin blocks were then prepared.
6. Subsequently sections of 4-6 micron thickness were cut from these blocks with the help of a microtome.
7. Sections were stained by Hematoxylin and Eosin stain.
8. Cover slip was placed and then mounted with DPX.
Examination of the slides were done under compound microscope both in 10x and 40x field. All the HPE tissues both benign and malignant were included in this study. Results were obtained in accordance with the WHO classification.

RESULTS
Total 471 cases were studied out of which 419 (89.15%) were benign and 52 (11.06%) were malignant. (Graphical presentation of age-wise distribution of number of benign

Graph-1: Shows percentage of age-wise distribution of benign lesions of female genital tract

Graph-2: Shows percentage of age-wise distribution of malignant lesions

Figure-1: Serous cystadenocarcinoma with papillary structures invading the stroma (shown by arrow mark); Figure-2: Granulosa cell tumour (100x) with nuclear pleomorphism and grooves in nuclei (shown by arrow mark); Figure-3: LSIL with nuclear membrane irregularities, nuclear hyperchromasia, nuclear halos, high N:C ratio (shown by arrow mark); Figure-4: CIN III with presence of dysplastic cells in upper third of lining of the cervix (shown by arrow mark); Figure-5: Keratinising squamous cell carcinoma of cervix with nests of neoplastic cells and well formed keratin pearls (shown by arrow mark)
Most common site of ectopic pregnancy is fallopian tube and Hematosalpinx 1 case was found in 60 years of age. Paratubal Cyst 2 cases were found in 24 and 25 years of age, 29 and 36 years. Parafimbrial Cyst 3 cases were found in 18, age group of 15-25 years. Paroovarian Cyst 2 cases found in 26-35 years, 12 cases in the age group of 36-45 years. Ectopic Pregnancy was found in 47 cases (16.54%). Age-wise distribution of the lesions of fallopian tube (70.42%) were normal.

Neoplastic Tumours- A total of 133 cases (56.84%) out of 234 specimen were found to have neoplastic changes.

Benign Epithelial Tumours- Total 117(50%) cases out of total 234 specimen with ovarian pathology were benign lesions. The various lesions in 15-25 years were serous cystadenoma (9); mucinous cyst adenoma (15); mature cystic teratoma (5), in 26-35 years: serous cystadenoma (13); mucinous cystadenoma (10); mature cystic teratoma (8), in 36-45 years: serous cystadenoma (14); mucinous cyst adenoma (22); mature cystic teratoma (4), in 46-55 years: serous cyst adenoma (4); mucinous cyst adenoma (6), in 56-65 years: serous cystadenoma (4); mature cystic teratoma (1), in 66-75 years: mucinous cyst adenoma (2).

Majority of lesions was found in the age group of 36-45 years i.e., around 40 cases (34.19%). Serous Cystadenoma was found in 44 cases (37.60%). Mucinous Cyst Adenoma was found in 55 cases (47%).

Germ Cell Tumours- Mature Cystic Teratoma was found in 18 cases (15.38%).

Fallopian Tube- Total 284 specimen were received, 200 specimen received were by total abdominal hysterectomy with some pathology in the corpus uteri and 84 specimen were by salpingoophorectomy. Out of these, 200 cases (70.42%) were normal.

Age-wise distribution of the lesions of fallopian tube

Ectopic Pregnancy was found in 47 cases (16.54%): 5 cases in the age group of 15-25 years, 30 cases in age group of 26-35 years, 12 cases in the age group of 36-45 years. Chronic Salpingitis was found in 28 cases (9.86%) in the age group of 15-25 years. Parovarian Cyst 2 cases found in 29 and 36 years. Paraovarial Cyst 3 cases were found in 26-35 years. Paratubal Cyst 2 cases were found in 24 and 25 years of age and Hematosalpinx 1 case was found in 60 years of age. Most common site of ectopic pregnancy is fallopian tube with incidence of 90%. Factors predisposing to high rate of ectopic pregnancy are increased prevalence of sexually transmitted diseases, contraception, assisted reproductive technology, tubal sterilization. Salpingitis is seen commonly in the reproductive age group due to ascending infection or via hematogenous route. Most common sequelae is ectopic pregnancy and infertility.

Endometrium-Total 386 cases, out of these 200 specimen were obtained by hysterectomy and 186 by endometrial biopsy. Patient usually presented with bleeding p.v., menorrhagia, abnormal Papanicolaou smear with atypical cells favouring endometrial origin. Out of these, abnormality was detected in 368 (95.34%) cases which had some pathology.

Different Lesions Of Endometrium Based On Age

Benign Lesions

The age wise distribution of various lesions were in 15-25 years: proliferative endometrium (5); secretory endometrium (4); disordered proliferative endometrium (1); endometriosis (1); acute endometritis (1), 26-35 years: proliferative endometrium (32); secretory endometrium (13); atrophic endometrium (2); endometrial hyperplasia with atypia (1); endometrial polyp (3), 36-45 years: proliferative endometrium (83); secretory endometrium (67); atrophic endometrium (15); disordered proliferative endometrium (4); endometriosis (3); acute endometritis (2), in 46-55 years: proliferative endometrium (8); secretory endometrium (30); atrophic endometrium (13); disordered proliferative endometrium (1), in 56-65 years: proliferative endometrium (8); secretory endometrium (2); atrophic endometrium (24), in 65-75 years: secretory endometrium (10); atrophic endometrium (20);>75 years: atrophic endometrium (4).

Proliferative Endometrium - 136 cases (36.95%) Secretory Endometrium 117 cases (31.79%) Atrophic Endometrium – found in 78 (21.19%) cases. Disordered Proliferative Endometrium was found in 6 (1.63%) cases. Endometriosis – found in 4 (1.08%) cases. Acute Endometritis 3 (0.81%) cases.

Endometrial Hyperplasia Without Atypia was found in 15 (4.08%) cases.

Endometrial Hyperplasia with Atypia was found in 3 (0.82%) cases. Disordered Endometrial Polyp was found in 5 (1.36%) cases.

Myometrium – Total 200 specimen were obtained from total abdominal hysterectomy and 28 specimen by myomectomy.

Atrophic Endometrium – found in 146 (64.03%) specimen. Around 146 (64.03%) specimen had abnormal findings.

Various Lesions Of Myometrium

Leiomyoma found in 128 cases (56.14%) Adenomyosis found in 16 cases (7.01%). Adenomyomatous Polyp found in 2 cases (0.87%). Cervix- Total 200 specimen were obtained in this study.

Age-Wise Distribution of Various Lesions of Endometrium

In 15-25 years: leiomyoma (2); in 26-35 years: leiomyoma (34); adenomyomatous polyp (2), in 36-45 years:
leiomyoma(75); adenomyosis (10), in 46-55 years: leiomyoma (13); adenomyosis (6), in 56-65 years: leiomyoma (4).

**Various lesions of cervix**

**Benign**— around 168(84%) cases were found to be benign.

**Chronic non specific cervicitis** - found in 155(77.5%)

Endocervical Polyp—found in 7(3.5%) cases

Stratified squamous dysplasia of cervix was found in 3(1.5%) cases.

**Age-wise distribution of various lesions of cervix**

In 15-25 years: CNSC (2), in 26-35 years: CNSC (53); endocervical polyp(2), in 36-45 years: endocervical polyp(5); in 46-55 years: CNSC (54); stratified squamous dysplasia (3), in 56-65 years: CNSC(43); 66-75 years: CNSC (1), >75 years: CNSC (2)

**Vagina**- Leiomysma was found in 1 case in 50 years of age.

**Vulva**- Fibroepithelial polyp 1, Bartholin’s cyst 1, hidradenoma papilliferum 1, mainly found in 15-25 years.

**Various malignant lesions in this study:** Total 52 malignant lesion were found.

**Ovary**

Borderline Tumours- Serous adenoma borderline was found in 1 case(0.75%) in 35 years of age.

**Malignant Tumours**- Patients with malignant tumour presented with mass per abdomen only or with distension abdomen. Total 15 cases (4.07%) were obtained. Grossly, the tumour size varied from 3-30cm. Around 8 specimen were from right ovary, 6 cases from left ovary, 1 case was bilateral. Serous cystadenocarcinoma was found in 10 cases(60%) with 1 case in 24 years of age, 2 cases in 26-35 years, 2 cases in 36-45 years, 2 cases in 46-55 years, 3 cases in 56-65 years.

**Mucinous Cystadenocarcinoma** found in 2 cases (13.33%) with 1 case in 48 years and 69 years. Moderately differentiated adenocarcinoma was found in 1 case(6.67%) in 52 years. Mixed germ cell tumour- was found in 1 case (6.67%) in 19 years. Granulosa cell tumour was found in 2 cases (13.33%) in the age group of 46-55 years.

**Endometrium**- Endometroid carcinoma in 2 cases (0.27%), found in 45 years.

**Cervix**- LSIL, CIN I, CIN III, each having 1 case (4.5%) in 35, 30, 47 years, respectively. Squamous cell carcinoma found in 32 cases (16%), 4 cases in 26-35 years, 6 cases in 36-45 years, 10 cases in 46-55 years, 7 cases in 56-65 years, 4 cases in 66-75 years, 1 case in >75 years.

**Vagina** - verrucous carcinoma 1 case found in 35 years, squamous cell carcinoma 1 case found in 62 years.

**Vulva**- squamous cell carcinoma 1 case in 54 years age.

**DISCUSSION**

Reproductive health issue is now on the global social agenda for upcoming years. Maternal morbidity is the only indicator till now to assess women’s health even though reproductive morbidity occurs more frequently and leads to high morbidity of women in our country. USG and FNAC are helpful in providing provisional diagnosis, but HPE is definitive as it helps us to know the extent of the tumour also. The surgical pathology reports provide the histopathological diagnosis and specific information related to prognosis and treatment. Specimens received in fresh state should be described before fixation since formalin alters the natural colour and consistency of tissue. The gross description must be precise and brief. The final diagnosis of a tumour should include its cell type, grade, location, extent as well as adequacy of the resection margins, presence of lymphatic or vascular invasion, and status of the regional lymph nodes.

In our setup the most important cause of morbidity in young age was inflammatory and in the older age both inflammatory and malignancy. In case of inflammatory lesion people usually presented with discharge per vagina, U-V prolapse, irregular menstruation. In case of malignancy usual presentation was growth over any part of the external genitalia, bleeding, p. v, pain, abdominal distension. Women usually present late with these symptoms due to social stigma, negligence, socio-economic factors, poor hygiene, poor follow up, etc. Ultimately by the time they reach the physician, some of them are in the advanced stage of the disease. Despite the availability of HPV vaccines, other affordable methods for early detection and treatment of cervical cancer, it still continues to be a serious health problem in India. The world age-adjusted incidence rate of cervical cancer is 7.9/100,000 population, which is lower than the incidence in South-East Asian region, 19.2/100,000 population.

**Ovarian lesions**

Ovary is the common site for neoplastic as well as non-neoplastic lesions and can present in childhood to postmenopausal age group. Both type of lesions often present with similar clinical and radiological features, whereas some patients do not have any significant symptoms until an advanced stage. Solitary follicular cysts are most common in the non-pregnant women of reproductive age group around the menarche and menopause. Cysts greater than 1cm in diameter is designated as cystadenoma. Malignancies are detected on histopathological examination in most cases. These tumours have characteristic growth pattern and specific nuclear characteristics (fig1 and2). The common non-neoplastic cystic lesions out of 234 specimen comprises 43.32% similar to the study done by Patil et al. (34.2%), Prakash et al. (41%). On gross examination, serous neoplasms showed uniloculated cyst filled with serous fluid and mucinous neoplasms showed multiloculated cysts filled with gelatinous material. The number of benign lesion in our study was 42.30%, similar to the study done by Prakash et al. (54%), Sawant et al. (35.71%). The slight variation in the result could be due to difference in the sample size. In our study most of the non-neoplastic lesions was found in the age group of 36-45 years (graph 1) with 57.73% with...
all lesions being cystic. Similar to the study done by Anand et al.12 Kanthikar et al.9, Sawant et al.15 in which maximum lesions were found in the 3rd and 4th decade age group. Peak incidence of epithelial benign tumours were in the age group of 36-45 years (41.41%)(graph 1) similar to the study done by Sarangan et al.14 and Patel et al.20 with peak incidence in 3rd and 4th decade. The incidence of serous cystadenofibroma, ovarian fibroma and mature cystic teratoma did not match with any of the studies.

Malignant lesions of ovary
Total malignant lesions of ovary were 15(29.09%) out of 52 malignant cases with serous cystadenocarcinoma in 10 cases (18.18%), with mucinous cystadenocarcinoma 2 cases (3.64%), granulosa cell tumour 2 cases (3.64%), mixed germ cell tumour 1 cases(1.82%), moderately differentiated tumour adenocarcinoma 1 case(1.82%), which was similar to the study conducted by Kanthikar et al.9 (malignant tumours of ovary were 20%, serous cyst adenocarcinoma 8.57%, mucinous cystadenocarcinoma 4.28%, mixed germ cell tumour 2.34%), Geeta et al.10 (malignant tumours were 21.36% with serous cystadenocarcinoma 4.27%, mucinous cystadenocarcinoma 2.56%), Prakash et al.13 (malignant tumours in 3.2% cases). The slight variation in the study was due to the difference in the study period and sample size.Majority of the lesions were above 45 years, similar to the study done by Kanthikar et al.9 in which majority of malignant lesions were in age above 40 years, Geeta et al.10 found majority of malignant lesions in 46-60 years and above 60 years.

Uterine lesions
Endometrium is a tissue which shows structural reorganization with each menstrual cycle in preparation for implantation, in the absence of which superficial layer is partially or completely shed and remodelled in preparation for next cycle. Oestrogen and Progesterone are required for these cyclical changes.

Total 386 specimen (obtained by total abdominal hysterectomy and biopsy) were received. In these cases patients usually presented with abnormal uterine bleeding. Out of these 36.95%were proliferative endometrium, secretory endometrium in 31.79%, atrophic endometrium in 21.19%, disordered proliferative endometrium in 1.63%, endometriosis in 1.08%, acute endometritis in 0.81%, endometrial hyperplasia without atypia and with atypia in 4.08% and 0.82% cases, endometrial polyp in 1.36% cases and endometroid carcinoma in 0.78% cases. This result was similar to the study done by Sujatha et al.11 (Proliferative endometrium in 30.6%, Secretory endometrium in 32.4%, disordered proliferative endometrium in 6.8%, endometrial hyperplasia without atypia and with atypia in 8.6% and 0.4%, endometrial polyp in 2.7%). Dayal et al.14 found (proliferative endometrium 48.51%, secretory endometrium in 29.46%, Atrophic endometrium in 14.18%, endometrial hyperplasia 5.03%, endometrial polyp in 1.83%). Nayak et al.15 (proliferative endometrium in 41.88%, secretory endometrium in 21.88%, atrophic endometrium in 2.5%, endometrial polyp in 0.62%, endometroid carcinoma in 1.25%). Mitali et al.18 found (proliferative endometrium in 43.30%, secretory endometrium in 23.40%, atrophic endometrium 10%).In our study proliferative endometrium is mostly found in 26-35 years, 36-45 years and 46-55yearswith 23.53%, 61.03% and 5.88% cases respectively majority of lesions in 4th and 5th decade (65%), similar to the study done by Katuwal et al.20 (in 20-40 years 34.2%, >40 years 60%, majority of cases in 24-63 years). In the present study hyperplasia was seen in perimenopausal age group also found in study by Katuwal et al.20 Mitali et al.18 found 37.9% in 4th - 5th decade, Panchal et al.17 found 47.83% cases in 4th – 5th decade. The reason for increase incidence of atypical uterine bleeding in this age group may be due to the fact that these patients are in their climacteric period. As woman approaches menopause cycle shortens and often becomes intermittently anovulatory due to decline in their number of ovarian follicles and increased resistance to gonadotrophic stimulation causes decline in the estradiol level which cannot keep the normal endometrium growing.18

In our study leiomyoma was found in 56.14% cases. Most commonly found in 3rd and 4th decade with 23.29% cases in 26-35 years, 51.37% cases in 36-45 years and 8.9% cases in 46-55 years, adenomyosis in 7.01%, adenomyomatous polyp in 0.87% cases, similar to the study done by Dayal et al.14 (leiomyoma 57.6%, adenomyosis 15.10%, 31-40 years had 41.21% leiomyoma cases, 41-50 years had 39.39% leiomyoma cases), Anjali et al.22 found (leiomyoma in 54.54%, adenomyosis 2.27%, 31-40 years had 42.10% leiomyoma, 41-50 years had 40.73% leiomyoma cases). Atrophy before menopause may occur due to mechanical pressure exerted by the nodular mass of leiomyoma, over the overlying nearby endometrium.21

Cervix
The cervix is lined by two types of epithelium, an outer squamous epithelium and inner columnar epithelium which secretes mucin and a transformation zone containing reserve/basal cells. The epithelium is susceptible to many pathological changes from inflammation to malignant transformation. The various risk factors for carcinoma cervix include age at first intercourse, increased parity, human papilloma virus infection, multiple sex partners(five times more common in commercial sex workers), cultural and religious factors (e.g., lower incidence in the Jewesses). Increased two fold risk of invasive and inter epithelial neoplasia of the cervix among smokers than non - smokers.21

Majority of the benign lesions was chronic non -specific cervicitis 77.5% similar to the study done by Srikanth et al.31 85.06%, higher than study done by Patel et al.30 32.2%. Endocervical polyp was found in 3.5% cases similar to Kumar et al.28 (2.9%), Patel et al.30 (3.2%). All the malignant lesions were squamous cell carcinoma 100%. Most of the cases were non keratinising squamous cell carcinoma. Premalignant lesions LSIL, CIN III, stratified squamous dysplasia cervix comprised of 4.5% cases, the incidence of these lesions did not match with any study because of longer
duration of study period taken in these studies. Chronic non specific cervicitis was commonly seen in 26-35 years (31.55%), 46-55 years (32.14%), 56-65 years (25.59%) similar to the study done by Kumar et.al.25 (21-30 years - 24.05%, 31-40 years - 35.13%, 41-50 years - 23.73%), Patel et.al.20 (41-50 years - 44.7%, 31-40 years 25%). Endocervical polyp was found in age group 30-40 years similar to study done by Srikanth et.al.31 in which 31-40 years had endocervical polyp.

All malignant lesions were squamous cell carcinoma most common in the 4th and 5th decade 53.12% (see graph 2) similar to study done by Kumar et.al.25 in which 4th and 5th decade had 55.26% cases in 4th and 5th decade, Puroshotam et.al.23 showed 95% of malignant cases as squamous cell carcinoma, with 40-49 years age consisting of 65.25% cases. According to the terminology proposed by LAST committee LSIL appear as CIN 1, CIN2 and CIN3 considered as HSIL. Mild, moderate and severe cervical dysplasia (CIN 1-3) respectively, are distinguished by dysplasia in lower one third, lower two-thirds, and full thickness of squamous epithelium24 as elicited in fig 3 and 4. With age there is decrease in the immune response leading to increase susceptibility to HPV infection causing carcinoma cervix. Most malignant lesions were found in the 3rd and 4th decade of life (graph 2).

CONCLUSION

Though malignancies are more common in the older age group, health and hygiene has a remarkable role. These lesions have not spared any age group, community and economic status, thus carcinoma of the female genital system has become a serious health concern. Most lesions in our study were benign and commonly found in reproductive age (15-45years) and malignant lesions were relatively less and more common in post reproductive age (>46 years).

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