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Original Research Paper

Pathology

HISTOMORPHOLOGICAL EVALUATION OF TUMOURS OF FEMALE GENITAL TRACT AND ITS CHANGE IN TUMOUR PROFILE OVER A PERIOD OF 12YRS IN A TERTIARY CARE REFERRAL HOSPITAL IN CHENNAI.

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ABSTRACT

Background: The most common cause of morbidity & mortality among females are due to cancers arising from female reproductive organs next to breast cancers. The most common sites include uterine cervix, corpus uteri & ovary followed by least common sites like vulva, vagina, fallopian tubes and gestational trophoblastic diseases.

Aim of the study:

1. To evaluate the trend in the profile of benign, premalignant & malignant lesions of female genital tract (FGT) tumours at primary tertiary care hospital in Chennai.
2. To study frequency, age distribution & diverse histomorphological spectrum of tumours of female genital tract.
3. To compare and analyze our data with other published studies in the literature.

Materials & Methods:

This cross sectional retrospective observational study was conducted at tertiary care gynaecological center at Chennai over a period of 12 years from Jan 2008 to Dec 2019. The medical records were retrieved, data analyzed and the results were expressed in descriptive statistics. **Results:** During the study period we received 44752 histopathological specimens out of which 12477 cases were gynaecological malignancies. Cervix uteri (66.38%) was the most common site followed by ovary (16.65%), corpus uteri (10.71%), gestational trophoblastic disease (4.13%), vulva (0.82%), vagina (0.36%), fallopian tube (0.02%), and vault carcinoma (0.93%). Squamous cell carcinomas were most common type of malignancy in cervix (93.15%), vulva (91%), vagina (82%) & vault (78%). Endometrial adenocarcinomas (81%) were more frequent tumour in corpus uteri while surface epithelial tumours constitute 78.72% of cases in ovary. For gestational trophoblastic disease, 78.25% of cases had complete molar pregnancy. 41-50yrs of age groups were commonly affected for cervical, ovarian & endometrial malignancies where as in vulval lesions the most common age group was 61-70yrs. In case of gestational trophoblastic disease the majority of patients were presented at 21-30yrs of age. **Conclusion:** This is one of the largest studies conducted with more than 10000 cases being reported in female genital tract. Cervical carcinomas are the leading gynecological malignancy followed by ovary & corpus uteri at our institute. There is a declining trend in the distribution of cases among cervical cancers were as there is an increasing trend in distribution of cases in other site like ovary & corpus uteri.

KEYWORDS : Female genital tract, cancer cervix, changing trends, squamous cell carcinoma.

INTRODUCTION:

Female genital tract (FGT) tumours constitute about 10% of all cancers and the second common site next to breast cancers[1] among females. They are the important cause for morbidity & mortality in females. Cervix uteri, ovary and uterine corpus were the most common site for development of malignancies followed by vulva, vagina, fallopian tubes, & gestational trophoblastic disease[2].

Incidence of these diseases varies among developing and developed countries. In developed countries endometrial and ovarian cancers were more common than cervical cancers. Though there are screening programmes available for cervical cancers, patients with malignancies at other sites usually present in advanced stage due to lack of awareness, low socioeconomic status and lack of availability of diagnostic facilities causing increase in cancer morbidity & mortality in developing countries[3].

In developed countries they have a well organized screening procedures, surveillance & regular follow up protocol which was not available in developing countries[4].

Aim & Objectives of the study:

1. To evaluate the trends in the profile of benign, premalignant & malignant lesions of female genital tract tumours at primary tertiary care center in Chennai, Tamilnadu, India.
2. To study frequency, age distribution and diverse histomorphological spectrum of lesions of FGT
3. To compare and analyze our data with other published studies in the literature.

MATERIALS & METHODS:

This cross sectional retrospective observational study was conducted over a period of 12yrs from January 2008 to December 2019 at Department of Pathology, Institute of Obstetrics & Gynaecology, Egmore, a primary referral center in Tamilnadu. The cases reported during these periods were retrieved from the records in our department. The data were analyzed statistically using Microsoft excel software and the results were expressed in descriptive statistics using simple percentage.

Inclusion criteria:

1. All cases of premalignant & malignant lesions of cervix & endometrium.
2. All cases of benign, borderline & malignant lesions of ovary
3. All cases of Malignant lesions of vulva, vagina, fallopian tube
4. All cases of Gestational trophoblastic diseases

Exclusion criteria:

1. All non neoplastic & benign lesions of cervix,

endometrium, vulva, vagina, fallopian tube & placenta.
2. All non neoplastic lesions of ovary.

Sample size: 12477 cases.

RESULTS:

Out of 44752 histopathological specimens, a total of 12477 (27.88%) cases represent various neoplastic lesions of female genital tract. Annual distribution of cases was depicted in chart 1.

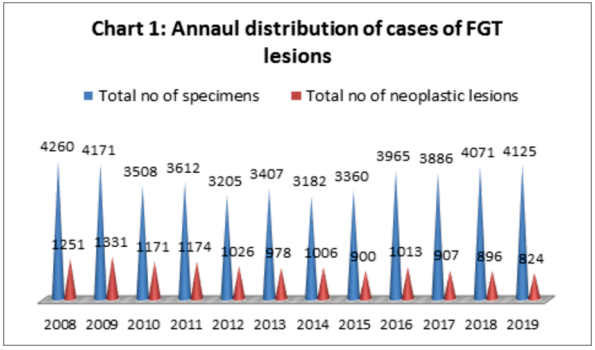


Chart 1: Annual distribution of cases of FGT lesions

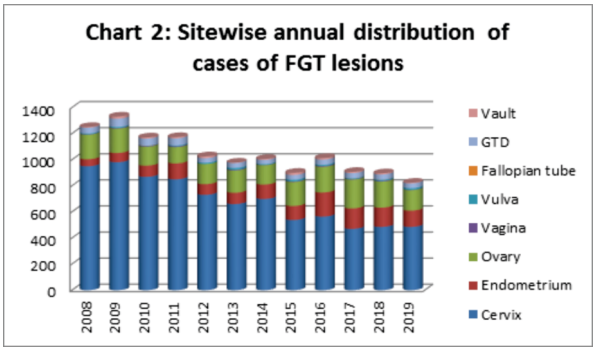
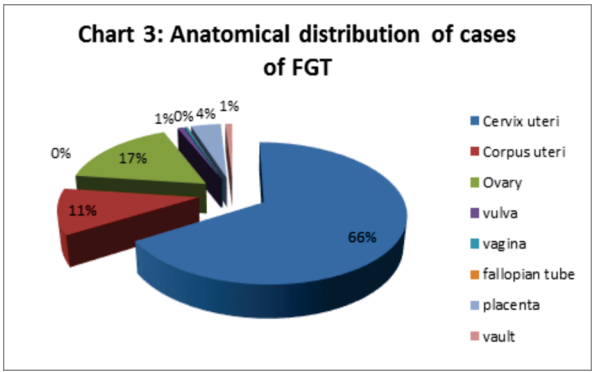


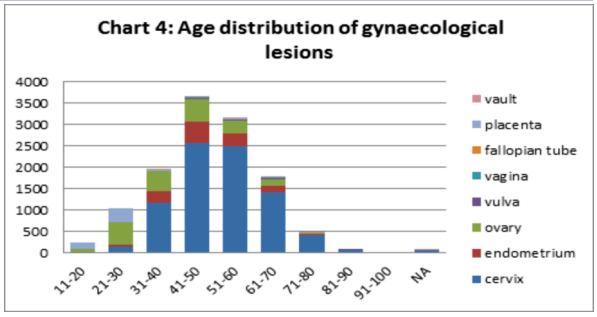
Chart 2 depicts site wise annual distribution of lesions of female genital tract.

Out of 12477 cases, 8282 (66.38%) were from cervix uteri, 2077 (16.65%) were from ovary, 1336 (10.71%) were from corpus uteri, 515 (4.13%) were from gestational trophoblastic disease, 102 (0.82%) were from vulva, 45 (0.36%) cases from vagina, 3 (0.02%) were from fallopian tube, 117 (0.93%) cases from vault biopsy as given in chart 3.



Age distribution:

In our study, we found that most common age group of presentation of female genital tract lesions was between 41-50 years with 3672 cases representing 29.43% of total cases followed by age group between 51-60 years accounting for 3166 (25.37)% cases. Age between 31-40 years & 61-70 years represented 1955 cases (15.67%) & 1778 cases (14.25%) respectively. Age group less than 20yrs represents 236 cases (1.89%) while least common age group of presentation belongs to 91-100 yrs with 10cases (0.08%).(Chart 4).

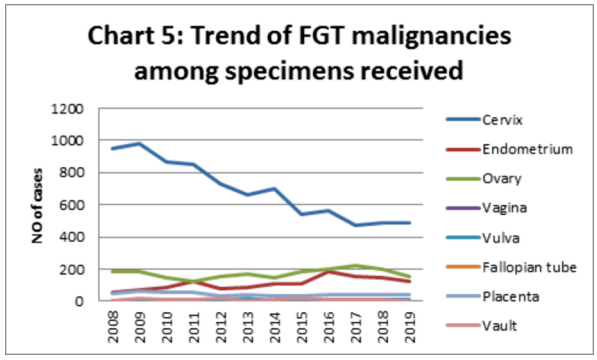


Cervix uteri were the most commonly affected site accounting for 66.38%. The mean age of patients with cervical cancer is 52.79yrs and the commonest age group falls under 51-60 yrs (2323 cases 31.44%) followed by 41-50yrs (2235 cases 30.25%), 61-70 yrs (1327 cases 17.96%). 79 cervical cancers were detected in patients younger than 30yrs of age. Out of 893 cases (10.78%) of premalignant lesions, 315 cases (35.27%) were in the age group of 41-50yrs followed by 31-40yrs of age (261cases, 29.23%), 51-60yrs (154cases 17.25%), 61-70yrs (87cases 9.74%), 21-30yrs with 62cases (6.94%). The common age groups of ovarian malignancies are 41-50yrs (524 cases 52.23%) with mean age of 39.99yrs. The common age groups for uterine tumours are 51-60yrs (218 cases 35.05%) with mean age 54.14 yrs. A total of 714 cases (10.78%) of premalignant lesions, 356 cases (49.86%) were in the age group of 41-50yrs followed by 31-40yrs (206cases 28.85%), 51-60yrs (85 cases 17.25%), 61-70yrs (29 cases 9.74%), 21-30yrs (62cases 4.06%).

102 cases (0.80%) of vulval carcinomas were identified with 61-70yrs (30cases 29.41%) of age were most commonly affected. 45 cases (0.36%) of vaginal carcinomas with 17 cases (38%) were in the age group of 51-60yrs. 3cases of fallopian tube and 117 cases of vault biopsies with 51-60yrs (42cases 36%) of age were commonly affected. 515 cases of gestational trophoblastic disease with 64.47% of cases falls within 21-30yrs of age followed by 11-20yrs (145cases 28.16%).

Trend of genital tract malignancies:

On analyzing the trend of genital tract malignancies among the specimens received at our institute over a period of 12yrs, there was decline in the proportion of cases in cervical malignancy where as there was increase in proportion of cases in ovarian malignancy followed by uterine lesions and gestational trophoblastic disease. At the same time there was no difference in distribution of cases in other sites over this period as shown in chart 5.



Histomorphological patterns of FGT lesions:

All tumours were classified based on WHO classification of tumours of female genital tract.

Distribution of cervical lesions:

Out of 8282 cases in cervix 893cases (10.78%) were premalignant lesions, 7389 cases (89.22%) were malignant lesions (Table 3). Cervical intraepithelial lesion (CIN) 3 were most common premaligant lesions while squamous cell carcinoma forms the most common form of cervical cancer

with 93.15% (6883 cases) followed by adenocarcinoma with 6.67% (493 cases) – Table 1 & 2.

Table 1: Distribution of cervical lesions:

Cervical lesions	Total no of cases	Percentage
Premalignant lesion	893	10.78%
1. CIN 1	307	34.38%
2. CIN 2	246	27.55%
3. CIN 3	337	37.74%
4. Adenocarcinoma insitu	3	0.33%
Malignant Lesions	7389	89.22%
1. Squamous epithelial lesion	6883	93.15%
2. Glandular lesion	493	6.67%
3. Mesenchyml tumours	9	0.12%
4. Metastatic tumours	4	0.05%

Table 2: Histological types of cervical tumours:

Histological types	Frequency	Percentage
Squamous epithelial lesions	6883	93.15%
1. Grade 1	377	5.48%
2. Grade 2	1760	25.57%
3. Grade 3	4746	68.95%
Glandular lesions	498	6.67%
1. Endocervical AdenoCA	361	73%
a. Endocervical type	287	79%
b. Endometrial type	35	10%
c. Mucinous type	31	9%
d. Papillary type	4	1%
e. Signet ring type	4	1%
2.Clear cell carcinoma	29	6%
3. Anaplastic carcinoma	53	11%
4. Adenosquamous carcinoma	28	6%
5. Carcinosarcoma	10	2%
6. Undifferentiated carcinoma	11	2%
7. Adenoid basal carcinoma	1	-
Mesenchymal tumours	9	0.12%
1. Leiomyosarcoma	8	89%
2. Embryonal RMS	1	11%
Metastatic tumours	4	0.05%

There was decrease in porportion of squamous cell carcinoma where as adenocarcinoma showed no change in distribution. As shown in chart 6.

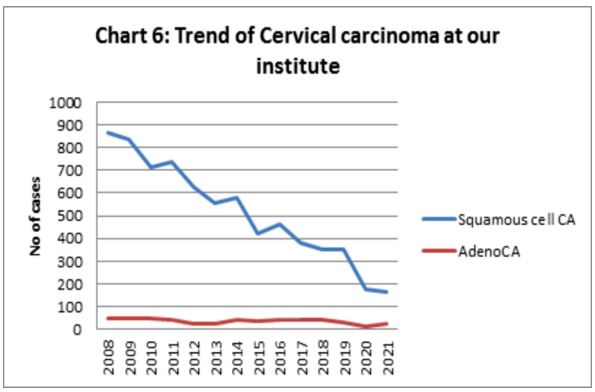


Chart 7: Trend of cervical carcinoma at our institute:

Distribution of lesions of uterine corpus:

Out of 1336 cases in corpus uteri, 714 cases (53%) were premalignant lesions, 622 cases (47%) were malignant lesions. Hyperplasia without atypia were most common premalignant lesions (623 cases, 87.25%) while epithelial tumours form most common uterine tumours (92.44%, 575 cases) followed by mesenchymal tumours (6.59%, 41 cases) – Table 3 ,4

Table 3: Distribution of uterine corpus lesions:

Uterine corpus lesions	Total no of cases	Percentage
Premalignant lesion	714	53%
1. Hyperplasia without atypia	623	87.25%
2. Atypical hyperplasia/EIN	91	12.75%
Malignant Lesions	622	47%
1. Epithelial tumours	575	92.44%
2. Mesenchymal tumours	41	6.59%
3. Mixed epithelial & mesenchymal tumours	3	0.48%
4. Metastatic tumour	1	0.16%
5. Gestational tumours	2	0.32%

Table 4: Histological types of uterine corpus tumours:

Histological types	Frequency	Percentage
Epithelial tumours	575	92.44%
1. Endometrial adenocarcinoma	501	87%
a. Endometroid	483	96%
b. Mucinous	9	2%
c. Villoglandular	9	2%
2. Papillary serous carcinoma	17	3%
3. Clear cell carcinoma	24	4%
4. Carcinosarcoma	26	4%
5. Mixed epithelial carcinoma	3	1%
6. Undifferentiated carcinoma	4	1%
Mesenchymal tumours	41	6.59%
1. Endometrial stromal sarcoma	30	73%
a. Low grade	28	93%
b. High grade	2	7%
2. Leiomyosarcoma	9	23%
3. Undifferentiated sarcoma	1	2%
4. Mixed smooth muscle & stromal tumour	1	2%
Mixed epithelial mesenchymal tumours	3	0.48%
Mullerian adenosarcoma	3	100%
Gestational tumours	2	0.32%
1. Choriocarcinoma	1	50%
2. Epitheloid trophoblastic tumours	1	50%
Metastatic tumours	1	0.16%

Distribution of ovarian lesions:

Out of 2077 cases from ovary epithelial tumours (1635 cases) were most common followed by germ cell tumours (305 cases), sex cord stromal tumours (125 cases), and metastatic tumours (11 cases) as shown in chart 7, table 5.

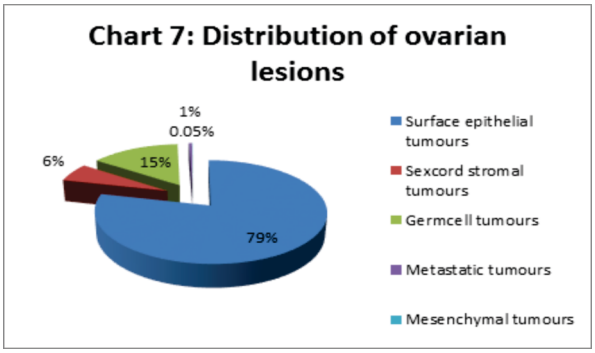


Table 5: Histomorphological spectrum of ovarian tumours

Ovarian lesions	No of cases	Percentage
Surface epithelial tumours	1635	78.72%
1. Serous tumours	1019	62%
a. Benign	792	77.72%
b. Borderline	36	3.53%
c. Malignant	191	18.71%
2.Mucinous tumours	469	27%

a. Benign	351	74.84%
b. Borderline	52	11.09%
c. Malignant	66	14.07%
3. Endometroid tumours	79	5%
a. Benign	14	17.72%
b. Borderline	4	5.06%
c. Malignant	61	77.62%
4. Seromucinous tumours	4	0.2%
a. Benign	1	25%
b. Borderline	1	25%
c. Malignant	2	50%
5. Brenner tumour	15	0.9%
a. Benign	14	93%
b. Borderline	1	7%
6. Clearcell carcinoma	18	1.1%
7.Carcinosarcoma	5	0.3%
8. Mixed cell adenocarcinoma	2	0.1%
9. Miscellaneous (Includes flui cytology & omental biopsies	25	0.01%
Sex cord stromal tumours	125	6.02%
1. Adult granulose cell tumour	46	36.80%
2. Juvenile granulose cell tumour	2	1.60%
3. Sertoli cell tumour	4	3.20%
4. Fibroma	23	18.40%
5. Thecoma	39	31.20%
6. Leydig cell tumour	1	0.80%
7. Sclerosing stromal tumour	2	1.60%
8. Steroid cell tumour	3	2.40%
9. Sertoli leydig cell tumour	5	4%
Germcell tumours	305	14.68%
1. Benign cystic teratoma	239	78.36%
2. Mature solid teratoma	2	0.66%
3. Immature teratoma	10	3.28%
4. Monodermal teratoma	3	0.98%
5. Mixed germ cell tumour	17	5.57%
6.Teratoma with malignant transformation	4	1.31%
7. Yolk sac tumour	8	2.62%
8.Dysgerminoma	22	7.21%
Metastatic tumours	11	0.53%

Table 6: Distribution of tumous from less common sites

Less common sites	Frequency	Percentage
Vulval lesions	102	0.82%
1. Epithelial tumours	100	98%
a. Vulval intraepithelial neoplasia	4	4%
b. Squamous cell carcinoma	91	91%
c. Adenocarcinoma	1	1%
d. Poorly differentiated carcinoma	1	1%
e. Anaplastic carcinoma	3	3%
2. Melanocytic tumours	1	1%
3. Hematolymphoid tumours	1	1%
Vaginal lesions	45	0.36%
1. Epithelial tumours	44	98%
a. Vaginal intraepithelial neoplasia	1	2%
b. Squamous cell carcinoma	36	82%
c. Adenocarcinoma	2	5%
d. Adenosquamous carcinoma	1	2%
e. Anaplastic carcinoma	2	5%
f. Adenoid cystic carcinoma	1	2%
g. Clear cell carcinoma	1	2%
2. Melanocytic tumours	1	2%
Vault lesions	117	0.94%
1. Epithelial tumours	116	99%
a. Carcinoma insitu	3	3%
b. Squamous cell carcinoma	91	78%
c. Adenocarcinoma	21	18%
d. Poorly differentiated carcinoma NOS	1	0%
2. Mesenchymal tumours	1	1%
a. Undifferentiated sarcoma	1	100%
Fallopian tube lesions	3	0.02%
1. Adenocarcinoma	2	67%
2. Carcinosarcoma	1	33%

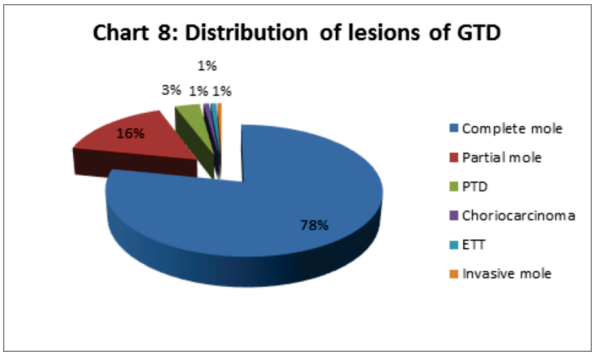


Chart 8 show distributions of lesions of 515 cases of gestational trophoblatic disease.

DISCUSSION:

According to Worldwide Globocan 2020 Fact sheet, cervical cancers were 4th most common tumours in women with 604127(6.5%) new cases, followed by uterine tumours which stand 6th with 417367 (2.2%) new cases, then ovary with 313959 cases, vulva with 45240 new cases & vagina with 17908 new cases[5,6]. In women breast and cervical cancers were most common cause of mortality. On observation there was a decline in the incidence and mortality rates of cervical cancers due to implementation of cervical cancer screening[7, 8], whereas the incidence rate of endometrial cancers were on increasing trend with fastest increase among younger generations[9]. In India, according to Globocan 2020 fact sheet, cancer cervix forms the second most frequent tumour among women with 123907 (8.3%) new cases followed by ovary (45701 new cases), corpus uteri (16413 new cases), vagina (5518 new cases) and vulva (3447 new cases)[10]. The trend of cancer cervix observed in 10 population based cancer registry showed a significant decrease in incidence by 1-2% annually with increase in incidence of uterine & ovarian cancers[11]. Similar trend of disease were also seen in Tamilnadu cancer registry[12].

Present study:

Our study were conducted in a tertiary care hospital situated at Chennai were we receive more than 3500-4000 gynaecological specimens per year. A 12 year study revealed a number of 12477 gynaecological malignancies including precancerous and cancerous lesions, recurrent tumours following hysterectomy or chemoradiation. Our study was one of the largest studies conducted in literature with large data of all types of tumours of FGT. The distribution of female genital tract lesions over a past 12 years showed a significant decrease in number of malignancies from 29.37% in 2008 to 27.88% in 2019.

Overall trend of female genital tract lesions:

In our institute cervix uteri were most commonly affected site for malignancy followed by ovary and uterine corpus followed by least common site like vulva, vagina, fallopian tube and gestational trophoblastic disease. Similar observations were made in other studies. Table 7 shows distribution of various female genital tract malignancies in comparison with other studies conducted over a period of 10years.

Table 7: Distribution of various FGT malignancies in comparison with other studies:

Author & Years	Total no of cases	Cervix	Ovary	Uterine corpus	Vulva	Vagina	GTD	Fallopian tube	Vault
Jamall 3 et al, 10yrs	968	231	411	162	53	43	-	1	-

Mohammed14 et al, 11yrs	513	395	43	52	6	16	-	1	-
Agarwal et al15, 10yrs	1315	927	196	129	35	9	-	1	-
Kyari et al16, 10yrs	1682	273	63	17	6	2	16	-	-
Hemalatha et al17, 10yrs	475	358	73	27	8	9	-	-	-
Present study	12477	8282	2077	1336	102	45	515	3	117

Overall age groups commonly involved in gynecological malignancies were in 41-50yrs with age ranged from 12yrs to 97yrs. This was consistent with the study done by kyari et al[16].

Among cervical lesions we included both premalignant and malignant conditions. There was increase in distribution of cases among premaligant lesion over 12 years with 3.3% detected in 2008 to 11% in 2019 due to implementation of cervical cancer screening procedures like PAP screening and colposcopy guided biopsy at our center. In the present study CIN 3 constitute 37.74% whereas other studies done by Saini et al[18] and Igho et al[19] high grade squamous intraepithelial lesions contributed 58% and 54.29% respectively. Squamous cell carcinoma (SCC) was the most common cervical cancer with 93.15% followed by adenocarcinoma with 6.67% which was similar in study conducted by Der et al[20] (SCC 90%, Adenocarcinoma 6%) and Odukuma et al[21] (SCC- 81.65%, Adenocarcinoma – 6.42%).

In our study among premalignant lesion over 12 years with 3% in the year 2008 to 8% in 2019 with maximum number of cases were seen in the year 2017 (99 cases 14%). Hyperplasia without atypia (87.25%) was more common which was comparable with other study conducted by Rao et al[22] over 16years. Similar findings were also noted in malignant lesions of uterine corpus (5.4% in 2008 to 11% in 2019) and maximum number of cases were reported in the year 2016 (14%).

Among ovarian lesions an increasing trend was noted in total no of cases however the histomorphological types did not show any change in the period of 12years. Similar findings are also seen in other studies done by Maurya et al[23] and Modi et al[24].

Primary fallopian tube carcinomas are very rare tumour comprising 0.14-1.8% of female genital tract malignancies with serous carcinoma being the most common type[25]. In our institute we had three cases of fallopian tube carcinoma, 2 cases of serous carcinoma and one case of MMMT.

Vulval carcinomas are rare tumour representing 4% of gynaecological malignancies & 0.6% of all cancers in women[26]. The present study included 102 cases of vulval carcinoma with squamous cell carcinoma (89%) being the most common tumour. Vaginal carcinoma constitutes less than 1% of all gynaecological malignancies.

The present study showed 0.36% with 45 cases being reported in our institute comparable with other studies done by Yagi et al[27] & Chhabra et al[28]. There was no significant change in distribution of cases among vulval & vaginal carcinomas over a period of 12 yrs.

Gestational trophoblastic disease constitutes less than 1% of all gynaecological malignancies[29]. We reported 515 cases of GTD with complete mole being the most common lesion in comparion with other studies[30]. There was only mild decrease in number of cases with 9% in 2008 to 7% in 2019 with maximum cases seen in the year 2009.

For Vault carcinoma, 98% of the primary tumours were from cervix and two cases were from ovary. There was mild increase in number of cases with maximum number reported in 2009 & 2015.

Limitations of the study:

The data presented in this study does not accurately represent the community prevalence rates as it is only a hospital based data and there were distribution of cases to other cancer center in and around Chennai.

CONCLUSION:

This is one of the largest studies conducted with more than 10000 cases being reported in female genital tract. Cervical cancers were most common tumours followed by ovary and uterine corpus. There was decreasing trend in proportion of cases in cervical cancer whereas there was increasing trend in proportion of cases in ovarian and uterine corpus tumours. There was not much difference in other least common sites like fallopian tube, vulva, vagina & vault carcinomas.

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