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**Original Research Article** 

# **Study of malignancies of reproductive tract in postmenopausal**

#### woman

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#### Abstract

Gynaecological malignancies are showing a trend of increase worldwide. In this observational study we tried to pick up the incidence, types, staging at presentation, common therapeutic modalities and follow up performance .Overall the study recruited around 1000 patients and span over a period of 3 years. It was conducted in the Eden Hospitals, Kolkata. The results were formulated and they more or less followed the standard rates. **Keywords:** Postmenopausal, malignancy, reproductive tract, RMT, palate.

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#### **1. Introduction**

Gynaecological cancer encompasses a number of tumors with different epidemiology, pathology and treatment strategies. Gynaecological cancer is the uncontrolled growth and spread of abnormal cells originating from the female reproductive tract – including ovaries, fallopian tubes, uterus, cervix, vagina and vulva. [1]

Like other parts of the body, the organs of the reproductive tract are made up of many types of cells. Cells divide in an orderly controlled way to produce more cells when they are needed in the body. When cells divide in an abnormal uncontrolled way, they can form a tumor that may be either benign or malignant. [1]

Malignant tumors are cancerous. Cancer cells can invade and damage tissues and organs near the tumor. Also cancer cells can break away from a malignant tumor in the reproductive system and spread to other organs in the abdomen and form new tumours. The cancer cells also can enter the lymphatic system on the bloodstream and spread to the other parts of the body. [1]

#### 1.1 Aims and objectives

1) To identify the common malignancies of the reproductive tract in postmenopausal women.

- 2) To map the age distribution of common malignancies of the reproductive tract in postmenopausal women.
- 3) To identify the extent of association between the established risk factors among the study population.
- 4) To enumerate the management modality applied on the selected cases.
- 5) To identify the prevalence of different stages during the time of presentation.

#### 2. Materials and methods

#### 2.1 Study area

Department of Obstetrics and Gynaecology, Eden Hospital, Medical College, Kolkata.

#### 2.2 Population

All the patients with confirmed menopause (i.e. FSH > 30 in 2 occasions 6 weeks apart) achieved either medically or surgically who are diagnosed with gynaecological malignancy.

**2.3 Study period:**  $1^{st}$  June 2015 to  $31^{st}$  May 2018 (36 months)

#### 2.4 Time period

1 – 12 months – Recruitment of cases

- 12-24 months Assessment of risk factors and application of the rapeutic model.
- 24 36 months Follow up

#### 2.5 Sample size: 1000 cases

#### 2.6 Inclusion criteria

- 1) Postmenopausal women;
- 2) Diagnosed cases of malignancies of the female reproductive tract confirmed by HPE.

#### 2.7 Exclusion criteria

1) Suspected cases of malignancies unless confirmed by HPE; 2) Associated malignancies in any other organ of the body (except metastasis from a primary which is located in the female reproductive tract.

#### 2.8 Study design

Observational longitudinal study.

#### 2.9 Parameters studied

1) Age at presentation;

- 2) Site, type and stage of different malignancies encountered.
- 3) Any established risk factor associated with the disease.
- 4) Modality of treatment applied in each case.
- 5) Follow up at months after completion of therapy.

#### 2.10 Study tool

- 1) Patient selection.
- 2) Histopathological examination.
- 3) Planning out the therapeutic model best suited for the patient.
- 4) Investigations.
- 2.11Study technique

The study was executed at the department of Obstetrics and Gynaecology, Eden Hospitals, Medical College, Kolkata.



#### 2.12 Analysis of data

Analysed using standard statistical protocols like prevalence, mean, median, proportion and p-value.

#### 3. Results and analysis

Total 1000 cases were recruited for this study. All patients were postmenopausal previously stamped from Menopausal Clinic, Eden Hospitals, Kolkata. After a proper history taking, clinical examination, some proper investigation were performed and a therapeutic model was executed for these patients. The patients were followed up at 1 yr after the therapy was applied.

### 3.1 General epidemiology

Table 1: Relative frequency of different malignancy		
Diagnosed case of	Frequency	Percentage
Ovarian carcinoma	260	26 %
Fallopian tube carcinoma	0	0%
Endometrial carcinoma	110	11%
Malignant mixed mullerian tumor	30	3%
Uterine sarcoma	10	1%
Cervical carcinoma	540	54%
Vaginal carcinoma	30	3%
Vulval carcinoma	20	2%
Total (n)	1000	100%

Table 1 Shows that cervical cancer predominated the incidence with a total of 54 % followed by ovarian carcinoma with 26 %. It was noteworthy that 3 cases of malignant mixed mullerian tumor, which is an otherwise rare tumor presented in the OPD during the period of recruitment.

Table 2. Age distribution of different mangnanetes							
Age (Vrs)	Ovarian	Cervical	Endometrial	Malignant Mixed	Uterine	Vaginal	Vulval
Age (113)	Cancer	Cancer	Cancer	Mullerian Tumor	Sarcoma	cancer	cancer
40 - 49	30	20	20	0	0	0	0
50-59	220	60	90	10	0	30	10
60 - 69	10	430	0	10	10	0	10
70.8	0	30	0	10	0	0	0

Table 2: Age distribution of different malignancies

Table 2 Shows that in between age 50 -59 majority of cases presenting were of ovarian malignancies where as in the group of 60 -69 it was cervical cancer as the major one.

#### 3.2 Ovarian cancer

#### Table 3: Age wise distribution of ovarian carcinoma

Age distribution (in yrs)	Number of cases
40 - 49	30
50 - 59	220
$\geq 60$	10

Table 3 Shows that the majority of cases of ovarian carcinoma were presenting at the age group between 50 to 59 yrs.

### Table 4: Relationship between early age of menarche and overien carrieneme

ovarian carcinoma		
Age of menarche < 12 yrs	Number of cases	
Yes	50	
No	210	

Table 4 shows that though there is a known association between early age of menarche and the incidence of ovarian carcinoma yet our study showed that in our series about 20% of cases had history of early menarche.

### Table 5: Relationship between delayed age of menopause and ovarian carcinoma

Late age of menopause (> 51 YRS)	Number of cases
Yes	90
No	170
	1 1 0.5.0

Table 5 Shows that in our study there was about 35 % of total cases had a history of delayed menopause which was quite significant as per as reference standards are considered.

#### Table 6: Relationship between hormone replacement therapy and incidence of ovarian carcinoma

History of hormone replacement Therapy for more than 5 yrs	Number of cases
Yes	10
No	250

Table 6 shows that in our study among 26 cases only one case had history of hormone replacement therapy which did not yield any significant result.

#### Table 7: Relationship between nulliparity and incidence of

ovarian carcinoma		
Nulliparity	Number of Cases	
Yes	50	
No	210	
	1 1 2 2 2 1	

Table 7 shows that approximately 20 % patients in our series were nulliparous which is a quite significant finding.

#### Table 8: Relationship between family history of cancer and incidence of ovarian carcinoma

inclucifice of ovarian carefulonia	
Family history of cancer	Number of cases
Yes	30
No	230

Table 8 shows that in our series only 3 cases gave a positive family history of cancer which gives approximately 12 % of occurrence among all cases.

#### Table 9: Relative incidence of different stages at presentation

Stages at presentation	Number of cases
la	20
1b	10
1c	90
2a	0
2b	0
2c	0
3a	0
3b	0
3c	100
4	40

Table 9 shows that in our series of ovarian carcinoma 12 cases presented at a relatively early stage while 14 cases presented at late stage.

#### Table 10: Comparison between different therapeutic modalities on the basis of follow up

Stage on	Therapeutic Modality	Incidence of recurrence in follow up
Presentation	(1>2)	(CA 125, CT scan, Phy. Exam, CXR PA)
1a	Surgery	0
1b	Surgery	0
1c	Surgery +Chemotherapy	20
3c	Chemotherapy+Surgery+ chemotherapy	20
4	Chemotherapy	40

Table 10 shows that in our series there was a recurrence rate of 20 % in both stage 1c & stage 3c tumors. All the patients with stage 4 tumors came up with recurrence at 12 months interval.

#### **3.3 Cervical carcinoma**

Table 11: Age wise presentation of cervical carcinoma

Age (in yrs)	Number of cases
40 - 49	20
50 - 59	60
60 - 69	430
$\geq 70$	30

Table 11 shows that the maximum number of cases of cervical carcinoma presented at the age group between 60 - 69 yrs which is a common age of presentation for this cancer as per reference standards.

#### Table 12: Relationship between multiparity (parity> 2) and

incidence	of cervical	carcinoma
Desites	Nerreel	have of an and

Parity	Number of cases
$\leq 2$	150
> 2	390

Table 12 clearly shows that there is association between multiparity and incidence of cervical carcinoma as more than 70 % of our cases had history of more than parity more than 2.

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Table 13: Relationship between history of early age of intercourse and incidence of cervical carcinoma

History of Early intercourse (< 16 yrs)	Number of cases
Present	110
Absent	430
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Table 13 shows that about 20 % of patients in our series had history of early intercourse (< 16 yrs) which is quite acceptable as per reference standards.

## Table 14: Relation between history of having multiple sexual partners & incidence of Cervical cancer

History of multiple Sexual partners	Number of cases
Present	150
Absent	390

Table 14 shows that in our series approximately 28 % of our cases had positive history about having multiple sexual partners which correlates very smoothly along the reference standards.

## Table 15: Relationship between tobacco intake & incidence of cervical cancer

History of tobacco intake	Number of cases
Present	110
Absent	430

Table 15 shows that in our series 20 % of the total number of cases had a positive history of tobacco intake which gives us a fine hint that tobacco addiction can be an associated factor in the epidemiology of cervical cancer.

## Table 16: Relationship between socio economic status & incidence of cervical carcinoma

Socio economic status	Number of cases
High	0
Middle upper	0
Middle	20
Middle lower	70
Lower	450

Table 16 shows that in our study as we divided our patients in different socio economic group according to Prasad's Scale what we got was that majority of our patients belonged to the lower socio economic group.

Table 17	: Relative	incidence of	f different	stages	at pre	sentation

Stages at presentation	Number of cases
1A	0
1B	30
2A	0
2B	260
3A	100
3B	110
4A	30
4B	10

Table 17 shows that the majority of cases of cervical cancer presented at a relatively late (inoperable) stage. Hence it signifies the fact that cervical cancer as per reference standards usually presents late.

Table 18: Comparison between different treatment modalities on the basis of follow up

Stage on presentation	Treatment Modality	Incidence of Recurrence (Dig. Exam. CT scan W/A)
1b	Surgery+ radiotherapy	0
2b	Radiotherapy	60
3a	Radiotherapy	70
3b	Radiotherapy	40
4a	Chemotherapy	30
4b	Chemotherapy	10

Table 18 signifies the fact that there was a recurrence rate of 23 % among **stage 2B** tumors treated with radiotherapy. It was 70 % among the **3A tumors** treated with radiotherapy. The recurrence rate was 37% among **3B tumors**. It was also note worthy that there were 3 cases presenting at **stage 1B** which were treated with surgery followed by radiotherapy and none of them had any recurrence at 6 months follow up period.

#### 3.4 Endometrial carcinoma

#### Table 19: Age wise presentation of endometrial cancer

Age group (in yrs)	Number of cases
40 - 44	0
45 - 49	20
50 - 54	60
55 - 60	30

Table 19 shows that the maximum number of cases which presented in this series belonged to the age group between 50 to 60 years which again is the most common age group for presentation of endometrial cancer as per reference standards are concerned.

#### Table 20: Relationship between nulliparity & incidence of

endomet	rial	car	cinoma	l

Nulliparity	Number of cases
Present	30
Absent	80

Table 20 shows that in our series about 27 % of patients with endometrial cancer were nulliparous.

## Table 21: Relationship between history of having irregular periods & incidence of endometrial cancer

History of having irregular periods	Number of patients
Present	4
Absent	7
Absent	7

Table 21 shows that in our series about 37 % of patients had history of irregular menstrual periods which again signifies the plot that unopposed estrogen activity plays an important role in the epidemiology of endometrial cancer.

### Table 22: Relationship between obesity (BMI $\geq$ 25) & incidence of endometrial cancer

BMI	Number of cases
≥25	2
< 25	9

Table 22 shows that in our series about 19 % of women with endometrial cancer were overweight.

# Table 23: Relationship between hypertension & incidence of endometrial carcinoma

Patients with hypertension	Number of cases		
Present	50		
Absent	60		

Table 23 shows that in our series about 45 % of patients with endometrial cancer were suffering from hypertension which brings a strong association between hypertension & endometrial cancer.

# Table 24: Relationship between diabetes mellitus & incidence of endometrial cancer

Patients with Diabetes mellitus	Number of cases	
Present	30	
Absent	80	

Table 24 shows that in our series about 27 % of cases of endometrial cancer were suffering from diabetes mellitus.

#### Table 25: Relative incidence of different stages at presentation

(surgical staging)		
Stages at presentation	Number of cases	
Stage 1	80	
Stage 2	10	
Stage 3	20	

Table 25 shows that as per reference standards in our series too, majority of cases of endometrial cancer presented at an early age (72 %).

Table 26: Comparison b	etween different treatme	nt modalities on the	basis of follow up

Stage at Presentation	Treatment Modality	Incidence of recurrence in follow up (Gen. Exa, CT scan)
1	Surgery +radiotherapy	0
2	Surgery +radiotherapy	0
3	Chemotherapy	10
1	4 4 1 4 0	C 11 11 11 d Cd

Table 26 Shows that in stage 1 & 2 tumors treated with Surgery followed by radiotherapy none of the cases showed recurrence in 12 months follow up. But in case of stage 3 tumors treated with chemotherapy 50 % showed recurrence at 6 months.

#### 3.5 Malignant mixed mulleriantumor

 Table 27: Age wise presentation of malignant mixed mullerian

tuillor		
Age group (in yrs)	Number of cases	
50 - 59	10	
60 - 69	10	
$\geq 70$	10	

Table 27 fails to show any light on the age presentation as there are equal members in the 3 age groups defined in our series. **Table 28: Relative incidence of different stages at presentation** 

Stage at presentation	Number of cases
1a	0
1b	0
1c	0
2a	0
2b	0
3a	0
3b	20
3c	0
4a	10
4b	0

Table 28 shows that in our series all the cases of malignant mixed mulleriantumor has presented late which is generally the nature of the tumor as per the report given by the reference standards.

 
 Table 29: Comparison between different treatment modalities on the basis of follow up

Stage on presentation	Treatment Modality	Incidence of recurrence in follow up
3b	Surgery	20
4a	Chemotherapy	10

Table 29 shows that as malignant mixed mulleriantumor is a highly aggressive tumor hence its aggressive nature is reflected on our study too. In our series too all 3 cases came up with recurrence at 12 months follow up.

#### 3.6 Carcinoma vagina

Table 30: Age wise presentation of vaginal carcinoma

	Age group (in yrs)	Number of cases	
	40 - 49	10	
	50 - 59	20	
Γ.	11. 20	1	

Table 30 gives us an idea that carcinoma vagina is a tumor which is more commonly occurring in the age group of 50 - 59 yrs. This also correlates with the fact provided by standard reference.

 Table 31: Relationship between history of having high risk

sexual behaviour & incidence of carcinoma vagina		
History of having high Risk sexual	Number of	
behaviour	cases	
Present	10	
Absent	20	

Table 31 shows that in our series about 33 % of our cases had a positive history regarding high risk sexual behaviour.

#### Table 32: Relationship between history of long term pessary use (> 10 yrs) & incidence of yaginal cancer

use (* 10 yrs) & merdence of vaginar cancer	
History of long Term pessary use	Number of cases
(> 10 yrs)	
Present	20
Absent	10

Table 32 Shows that in our series about 66 % of patients had a positive history regarding long term pessary use (> 10 yrs).

Table 33: Relative incidence of different stages at presentation

Stages at presentation	Number of cases
1	0
2	0
3	30
4	0
-1.1. 22 -1 41	

Table 33 shows that in our series all the 3 cases of vaginal carcinoma presented at stage 3 which again gives strong evidence towards the fact that vaginal carcinoma is a late presenting tumor.

#### Table 34: Comparison between different treatment modalities on the basis of follow up

Stage on presentation	Treatment Modality	Incidence of recurrence in follow up (Dig. Exam, CT scan W/A)
3	Radiotherapy	0

Table 34 shows that in our series all the 3 patients presenting at stage 3 were treated with radiotherapy and none of them came up with a recurrence.

#### 3.7 Carcinoma vulva

 Table 35: Relative incidence of different stages at presentation

Number of cases
20
0
0
0

Table 35 shows that in our series all the cases presented quite early at stage 1.

#### Table 36: Comparison between different treatment modalities on tha basis of follow up

Stages at presentation	Treatment Modality	Incidence of recurrence in follow up (CT scan W/A Dig. Exam.)
1	Surgery	0

Table 36 shows that in our series both the cases were treated with surgery and none of the cases reported any recurrence at 12 months follow up.

#### 4. Discussion

In the above mentioned study total 1000 patients were selected. All the patients were postmenopausal as documented by their history. All the patients were suffering from malignancies of the female reproductive tract.

The malignancies which we took mainly into account were:

- Ovarian malignancy
- Fallopian tube malignancy
- Endometrial malignancy
- Malignant mixed mulleriantumor
- Uterine sarcoma
- Cervical malignancy
- Vaginal malignancy
- Vulval malignancy

The relevant facts about these malignancies regarding their relative incidence, age wise distribution, association with different risk factors, efficacy of different treatment modality which came into the limelight through our study will henceforth discussed in the following paragraphs.

As it has been made evident in table 1 our study showed that cervical malignancy had the maximum share in incidence with a whooping 54 % in its tally. It was followed by ovarian malignancy with an incidence of 26 %. What was quite noteworthy that within a span of 12 months during the time of recruitment 30 cases of malignant mixed mullerian tumor were recruited in the study which is an otherwise rare tumor .This comes in well correlation with the work of Uma devi where she also found the incidence of cervical cancer to be approximately 65 % of population in this age group.[2]

As per age distributions are concerned from table 2 we came into the conclusion that in between 50 - 59 yrs it was ovarian cancer which predominates. After age of 60 yrs it is however it is cervical malignancy which takes its largest share. This results once again corroborates well with the study done by Jemal A. where they reported a peak incidence of cervical cancer in the age group between 60 - 65 yrs. [3]

This result also shares its view with the work done by Berek JS where they showed that the peak incidence of invasive epithelial cancer of the ovary is between 56 to 60 yrs. [4]

Henceforward for our discussion purpose we will divide our topic under subheadings to brief the results which we obtained about different malignancies.

#### 4.1 Ovarian malignancy

As per as table 3 is concerned we can safely conclude that from our study the age of occurrence for epithelial ovarian carcinoma appeared to be between 50 to 59 yrs. This comes in accordance with the work done by Pecorelli *et al*, who also concluded that peak age of incidence for epithelial ovarian carcinoma is also 50 to 59 yrs.[5]

All cases obtained in our study were of epithelial ovarian malignancy by nature. IJBR (2020) 11 (03) Pag If we come across table 4 we would find that though there is a known association between early age of menarche & ovarian carcinoma yet in our study finds that only 20% of our patients had history of early menarche. It corresponds with the value given by Franceschi S about the relation between age of menarche & incidence of epithelial ovarian cancer.[6]

If the results of table **5** are considered then we will find that in our series there was 35% of our total cases who had history of delayed menopause which is in accordance with the work done by La Vecchia C on the same topic. [6]

When the results of table 6 are considered we wouldn't find any association between history of hormone replacement therapy (> 5 yrs) & incidence of epithelial ovarian carcinoma. This was most probably due to the fact that as the maximum number of our patients belonged from lower socio economic strata hence they couldn't afford the price of Hormone Replacement Therapy. Hence the relationship between HRT & incidence of epithelial ovarian carcinoma couldn't be established by our series.

According to table 7 20 % of all the patients in our series were nulliparous which again comes in accordance with the results demonstrated by Negri E who also showed similar results with his study. [7]

If the results of table 8 are considered then in our series about 12 % of our cases had family history of malignancy which again comes in accordance with the work done by Whittemore AS, where they also found about 10 % of patients in their series had positive family history of cancers. [8]

Table 9 throws light on the relative incidence of different stages at presentation where we find that about 46 % of the cases were presenting at stage 1.54% cases presented relatively late.

Table 10 analyses the treatment modalities applied on selected cases. According to this table we can see that the treatment modality applied in our series were quite effective in the early stages. Only 16% of all the cases diagnosed in stage 1 reported a recurrence at 6 months interval. 20% cases diagnosed of stage 3C (treated with neoadjuvant chemotherapy) came back with relapse at 12 months interval. These results were in accordance with study by Trimble EL, who also reported similar follow up result in their study.[9]



Figure 1: Cut section of a specimen of mucinous cystadenocarcinoma in our series



Figure 2: Mucinous cystadenocarcinoma- Low Power Field



Figure 3: Cut section of a specimen of serous cystadenocarcinoma in our series



Figure 4: Serous cystadenocarcinoma – low power field

#### 4.2 Cervical cancer

In Table 11 we analyzed the age wise distribution of cervical carcinoma and we came to the conclusion that in our study the maximum number of cases presented at the age group between 60 to 69 yrs. This was again in accordance with the work done by Jemal A & Tiwari RC who also detected a peak in the incidence at the age group between 60 to 64 yrs.[10]

In Table 12 the association between multiparity& cervical cancer incidence was proved quite effectively as in our study about 70 % of patients suffering from cervical cancer were multiparous. This finding once again came in accordance with the work done by Jonathan S. Berek who also included high parity as an established risk factor for cervical cancer [10].

Table 13 gives us a hint that about 20 % of cases in our series had a history of early intercourse & were suffering from cervical cancer. This result was very much similar to the work done by Jonathan *et al* who again included history of early intercourse as an independent risk factor for cervical cancer.[11] Table 14 shows us that in our series about 28 % of cases had history of multiple sexual partners which again comes in accordance with the work done by Fu YS who also contributed that history of having multiple sexual partners is an important risk factor in the pathogenesis of cervical cancer.[10]

Table 15 shows that in our series there was a history of tobacco addiction among 20 % of patients which comes in conjunction with the work done by Jonathan S. Berek who again included cigarette smoking as one of the risk factors in cervical cancer. [12]

Table 16 gives us a clear proof of the work done by Jonathan S. Berek who showed that patients coming from the lower socio economic strata have clearly an increased risk for cervical carcinoma. In our series about 84% of patients belonged from the lower socioeconomic strata.[13]

In Table 17 we can see that when the relative incidence of different stages are plotted there is a predominance of presentation at stage 2B & 3B.This again comes in accordance with the work done by Avrette HE who showed the relative incidence of stage 2 & 3 tumors to be of 32% & 26% respectively.[14]

After analyzing Table 18 the fact which came surfaced was that in our series there was about 23 % recurrence in stage 2B & 33 % in stage 3 & this result was also in accordance with those given by Pettersson F who described a 60% cure rate for stage 2 & 45 % for stage 3 tumors. 30 cases presenting at stage 1B which were treated with surgery followed by radiotherapy and none of them had any recurrence at 12 months follow up period.[15]



Figure 5: Specimen of squamous cell carcinoma after resection in our series



Figure 6: Invasive squamous cell carcinoma of cervix -high power field

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#### 4.3 Endometrial cancer

In table 19 the underlined fact which was revealed from our study was that the principal age group of people suffering from endometrial cancer was between 50 to 60 yrs. This again comes in concurrence with the work done by Smith M who also documented that 75% of cases of endometrial carcinoma occur in women older than 50 years of age.[16]

According to the data provided by table 20 27% of our cases were nulliparous. This data again comes in smooth correlation with the work done by MacMohan B who concluded that nulliparous women have 2 to 3 times increased risk of endometrial cancer than parous women.[17]

None of the cases in our series yielded any positive history regarding any family history of HNPCC or menopausal hormone therapy.

Table 21 shows that in our series among all women suffering from endometrial cancer 37 % gave history of having irregular periods. This also correlates smoothly with the work done by Parazzini who also came to the conclusion that a history of irregular periods due to anovulatory cycles increases the risk of endometrial cancer.[18]

Table 22 shows that in our series about 19 % of women were obese. This gives a strong support to the fact that obesity is a risk factor in the incidence of endometrial cancer as was proved by Parazzini.[18]

Table 23 gives us the fact that in our series about 45 % of patients were suffering from hypertension along with endometrial carcinoma. This finding comes in smooth correlation that hypertension is an important associated factor with endometrial cancer as oroved before by Parazzini.[18]

Table 24 gives us the hint that in our series about 27 % of patients with endometrial cancer were suffering from diabetes mellitus. This again forms a strong support to the work done by Parazzini.[18] who concluded that diabetes mellitus increases a women's risk for endometrial cancer by 1.3 to 2.8 times.

Table 25 shows that in our series majority of the cases of endometrial cancer (72 %) presented at an early age. This was most probably due to the fact that there was relatively easy access to some important diagnostic tools in this disease.

Table 26 shows that in our series none of the cases treated with surgery followed by radiotherapy showed any recurrence within 12 month period. These results again correlate well with those done by Podczaski E who also encountered similar rates in his study. [19]



Figure 7: Cut section of a specimen of endometrial carcinoma in our series



Figure 8: Endometrial cancer - high power field

#### 4.4 Malignant mixed mullerian tumor

Though according to the work done by Norris *et al*, it was concluded that MMMT is a tumor occurring principally at an older age group, yet in our series table 27 failed to throw any light on this matter due to a relatively small sample size in our series.[20]

Table 28 showed that in accordance with the work done by Inthasorn *et al*, malignant mixed mullerian tumors are a group of highly aggressive tumors hence they always tend to present in a relatively advanced state which was also evident in our series. [21]

Table 29 also reflects on the highly aggressive nature of the tumor. Here we can see that all the 3 cases reported in our study came back with a recurrence within the 12 month period. This work again goes in the same line as the work done by Inthasorn *et al* on this topic **.**[21]



Figure 9: Specimen of MMMT in our series with heterologous differentiation



Figure 10: MMMT - High power field

#### 4.5 Uterine sarcoma

In our series we received only a single odd case of uterine sarcoma. The tumor was leiomyosarcoma by histopathological nature. The patient was 62 yrs old & she was nulliparous. This didn't match with the view given by Taylor HB who concluded that the median age for occurance of this tumor was 43 to 53 years. [22]

The patient presented did not have any history of exposure to radiation. This was contradictory with the work done by Czesnin who estimated the relative risk of uterine sarcoma after pelvic radiotherapy to be 5.38.[23]

The patient presented on stage 2A & was treated with surgery followed by radiotherapy. The patient didn't have any recurrence after 12months.But according to Salazar OM, it was concluded that recurrences develop in more than half cases of uterine sarcoma, even when the disease is apparently localized at the time of treatment.[24]



Figure 11: Cut surface of a specimen of uterine sarcoma in our series



Figure12: Leiomyosarcoma - Low power feild

#### 4.6 Carcinoma vagina

Table 30 gives us an idea that in our series majority of cases reported at an age group between 50 to 59

yrs. This report comes in line with the report published by Norris *et al*, who reported that mean age of patients with squamous cell cancer of vagina is 60 yrs [24].

All the 3 cases obtained in our series belonged to squamous cell carcinoma by histopathology.

According to Table 31 in our study about 33% of patients reported to have history of high risk sexual behaviors. In Table 32 we came across the fact that in our study about 66 % of the patients had history of long term pessary use for more than 10 yrs. All these results were in accordance with the results obtained by Ledward RS.[25]

According to Table 33 all of our cases presented at stage 3 hence we can safely decipher that carcinoma vagina usually presents late. This view get extra boosted by the work done by Benedet JL who found that 75 % of vaginal carcinoma presents between stage 2 to stage 4.[26]

Although the survival rates for carcinoma vagina has been described exceptionally poor by Jones RW yet in our series all the 3 patients were treated with radiotherapy yet none of them came up with features of any recurrence at 12 months follow up.[27]



Figure 13: Well differentiated squamous cell carcinoma of vagina – High power feild

#### 4.6 Carcinoma vulva

Table 35 shows that all cases of carcinoma vulva presented at a relatively early stage. Among the 20 cases ten were squamous cell carcinoma & ten were aggressive angiomyxoma of the vulva. There were no histories of Lichen sclerosis or atypical moles in any of the above mentioned cases in our series.

Table 36 showed that both the cases were treated with surgery and none of them came up with recurrence at 6 month follow up. All these results comes in conjunction with the work done by Jones RW regarding this matter.[28]



Figure 14: A case of huge aggressive angiomyxoma of vulva obtained in our series



Figure 15: Angiomyxoma - High power feild

#### **5.** Summary

Malignancies of the female reproductive tract encompass a number of tumors with different etiology, epidemiology & treatment strategies. Gynaecological malignancies are one of the commonest reasons for female mortality in the elderly age group. Though in recent years, much information has been gathered, our knowledge about the different gynaecological malignancies is still incomplete and confusing.

Malignancies of the female reproductive tract are a huge area with numerous corners yet to be explored. This study was initiated with the basic intention of exploring these areas as much as possible with our very own humble effort.

The study was done in the department of Obstetrics & Gynaecology, Medical College and Hospital, Kolkata. Patients who met the inclusion criteria and were exempted from the exclusion criteria were included randomly into the study from the outpatients department. Total 100 cases were included in the study. The study period span from 1<sup>st</sup> June 2015 to 31<sup>st</sup> May 2018. The total study period was divided into 3 separate periods for the purpose of operational advantage. For the initial 12months cases were recruited randomly from the outpatients department. Next 12 months were spent to chalk out different treatment modalities best suited for these patients & their application. The patients were followed up after 12 months in the outpatients department once again.

The facts found and observations made in the course of the study can be summarized as follows:-

- Among all the malignancies of the reproductive tract in post menopausal women cervical malignancy was the commonest one in our study with a whooping 54 % under its tally.
- It was followed by ovarian malignancy with an incidence of 26 % under its belt. Endometrial cancer was relatively rare in our study with a mere 11% incidence.
- When we came across the age wise distribution it was ovarian malignancy which predominated in the age group between 50 to 60 yrs where as cervical malignancy predominated between 60 to 69 yrs.

#### **Ovarian malignancy**

- All the cases obtained in our series of ovarian malignancy were epithelial type of malignancies from the point of histopathology.
- In our series maximum number of cases obtained who were suffering from epithelial ovarian cancer were from the age group between 50 to 59 yrs. Among these patients about 20% were nulliparous.
- Among patients suffering from epithelial ovarian carcinoma 20% had history of early menarche & 35 % had history of delayed menopause.
- Among all these patients about 12% of patients had positive family history of malignancy.
- Among all the patients we received with this disease about 46% presented at stage 1 and were treated successfully with surgery followed by 6 cycles of chemotherapy with a minimal recurrence rate at 12months interval. About 38% of tumors presented at stage 3c and were treated successfully with neoadjuvant chemotherapy followed by surgery.

#### **Cervical malignancy**

- All the cases obtained in our series of cervical malignancy were squamous cell carcinoma type from the point of histopathology.
- As per as age distribution is concerned about 80 % of cases presented in the age group between 60 to 69 yrs.
- In our study about 70 % of patients suffering from cervical cancer were multiparous.20% of all patients had history of early intercourse and 28 % gave a positive history regarding multiple sexual partners in our study. In our study about 84% of patients with cervical cancer belonged to lower socio economic strata and 20 % of these patients had history of tobacco addiction.
- In our study majority of the cases presented at stage 2B (48 %) & 3B (21 %). These patients were treated with radiotherapy with a 23 % recurrence rate in stage 2B, 70% in stage 3A and 37% among 3B tumors. There were 3 cases received at stage 1B who were treated with surgery followed by radiotherapy and none of them came up with a recurrence at 12months interval.

#### **Endometrial carcinoma**

- In our series about 80% of patients with endometrial cancer were from the age group between 50 to 59 yrs.
- Among all the patients with this disease about 27 % were nulliparous & 37 % gave history of having irregular menstrual periods.
- Among all the patients in our series in our series about 19 % of women were obese. About 45 % of patients were suffering from hypertension & 27 % of patients with endometrial cancer were suffering from diabetes mellitus.

• In our series about 72% of patients with endometrial cancer presented at an early stage (stage 1). All these patients were treated with surgery followed by radiotherapy and none of them came back with recurrence at 6 months interval.

#### Malignant mixed mulleriantumor

- In our series we received 30 cases of malignant mixed mullerian tumor which is an otherwise relatively rare tumor.
- All these cases presented at a relatively late stage reflecting the aggressive nature of the tumor.
- Among these 30 cases 20 were treated with primary surgery and other one with chemotherapy but they all came back with recurrence at 12months interval.

#### Uterine sarcoma

- In our series we received only ten cases of uterine sarcoma.
- The patients were all between 60-65 yrs old & they were nulliparous.
- The tumors were leiomyosarcoma by histopathological nature.
- The patients presented did not have any history of exposure to radiation.
- The patients presented on stage 2A & were treated with surgery followed by radiotherapy. The patients didn't have any recurrence after 12 months.

#### Vaginal carcinoma

- All the 30 cases obtained in our series belonged to squamous cell carcinoma by histopathology.
- Majority of cases of vaginal carcinoma were reported between the age group of 50 to 59 yrs.
- In our series of vaginal carcinoma about 33% of patients had history of high risk sexual behavior and 66% had history of long term pessary use for more than 10 yrs.
- All the 30 cases presented at stage 3 and were treated with radiotherapy as per convention
- And none of them came up with any recurrence at 12 months interval.

#### Vulval carcinoma

- Among the 2 cases one was squamous cell carcinoma & another one was an aggressive angiomyxoma of the vulva.
- In our series both the cases presented at an early stage.
- Both the cases were operable on presentation hence both of them were treated with surgery and none of them came back with a recurrence after 12 months.

#### 6. Conclusion

Malignancies of the reproductive tract itself are a huge topic with numerous twists and turns at appropriate places. The salient feature about different malignancies which came out as a result of our study was that: - In our study the commonest malignancy was cervical malignancy followed by ovarian malignancy.

As far as age distribution is concerned ovarian carcinoma predominated at the age group between 50 to 59 yrs where as cervical carcinoma predominated in the age group between 60 to 69 yrs.

Regarding ovarian malignancy, 20% were nulliparous, 20% had history of early menarche & 35 % had history of delayed menopause. About 12% of patients had positive family history of malignancy. 85% presented at stage 1 and were treated successfully with surgery followed by 6 cycles of chemotherapy with a minimal recurrence rate at 6 months interval. About 38% of tumors presented at stage 3c and were treated successfully with neoadjuvant chemotherapy followed by surgery.

Regarding cervical malignancy, about 80 % of cases presented in the age group between 60 to 69 yrs. About 70 % of patients were multiparous. 20% of all patients had history of early intercourse and 28 % gave a positive history regarding multiple sexual partners. About 84% of patients with cervical cancer belonged to lower socio economic strata and 20 % of these patients had history of tobacco addiction. Majority of the cases presented at stage 2B (48 %) & 3B (21 %). These patients were treated withradiotherapy with a 23 % recurrence rate in stage 2B, 70% in stage 3A and 37% in stage 3B.

Regarding endometrial carcinoma, about 80% of patients with endometrial cancer were from the age group between 50 to 59 yrs. About 27 % were nulliparous & 37 % gave history of having irregular menstrual periods. About 19 % of women were obese .About 45 % of patients were suffering from hypertension & 27 % of patients with endometrial cancer were suffering from diabetes mellitus. About 72% of patients with endometrial cancer presented at an early stage (stage 1). All these patients were treated with surgery followed by radiotherapy and none of them came back with recurrence at 6 months interval.

Regarding malignant mixed mulleriantumor, 30 cases of malignant mixed mulleriantumor were recruited in our study. All of whom presented presented at a relatively late stage. Among these 30 cases 20 were treated with primary surgery and other one with chemotherapy but they all came back with recurrence at 12months interval.

# Regarding uterine sarcoma, we received only ten cases of uterine sarcoma

The tumors were leiomyosarcoma by histopathological nature. The patients were between 60-65yrs old & they all were nulliparous. The patients presented did not have any history of exposure to radiation. The patients presented on stage 2A & were treated with surgery followed by radiotherapy. The patient didn't have any recurrence after 12 months.

Regarding carcinoma vagina, majority of cases of vaginal carcinoma were reported between the age group of 50 to 59 yrs. About 33% of patients had history of high risk sexual behavior and 66% had history of long term pessary use for more than 10 yrs.

All of the cases presented at stage 3 and were treated with radiotherapy as per convention and none of them came up with any recurrence at 6 months interval.

Regarding vulval carcinoma, there were 2 recruited cases and among them one was squamous cell carcinoma & another one was an aggressive angiomyxoma of the vulva.

Both the cases presented at an early stage and were operable on presentation hence both of them were treated with surgery and none of them came back with a recurrence after 6 months.

However this was a humble effort done for a small period of time with small number of patients. There is ample scope for further elaborate study in this field.

Larger endeavors with large sample size will probably reveal more important fact regarding the malignancies of the reproductive tract in post menopausal women.

#### References

- [1]. HC Kitchner, Postgrad Med. J 1999; 75: 332 338.
- [2]. K. Uma Devi. Current status of gynecological cancer care in India, J Gynecol Oncol. 2009 June; 20(2): 77– 80.
- [3]. Jemal A, Tiwari RC, Murray T, Cancer statistics, 2006, *CA Cancer J Clin* 2006; 56:106-130
- [4]. Berek JS, Hacker NF, Practical gynecologic oncology, 4<sup>th</sup> ed. Philadelphia, PA: Lippincott Williams & Wilkins, 2005; 443 – 541.
- [5]. Pecorelli S, Odicino F, Maisonneuve P, et al. Carcinoma of the ovary. Annual report on the results of treatment of gynaecological cancer. J Epidemiol Biostat 1998; 3 (23): 75 – 102.
- [6]. Franceschi S, La Vecchia C, Booth M, *et al.* Pooled analysis of three European case control studies of epithelial ovarian cancer. Age at menarche and menopause. *Int J cancer* 1991; 49:57-60.
- [7]. Negri E, Franceschi S, Tzonou A, et al. Pooled analysis of three European case control studies of epithelial ovarian cancer: I. Reproductive factors and risk of epithelial ovarian cancer. Int J Cancer 1991; 49: 50 -56.
- [8]. Whittemore AS, Gong G, Itnyre J. Prevalence and contribution of BRCA1 mutations in breast cancer and ovarian cancer: results from three U. S population based case control studies of ovarian cancer. Am J Hum Genet 1997; 60: 496 – 504.

- [9]. Trimble EL, Kosary CA, Cornelison TL, *et al.* Improved survival for women with ovarian cancer. *Procam Soc Gynecol Oncol* 1999: 136.
- [10]. Jonathan S. Berek. Berek & Novak's Gynaecology, 14<sup>th</sup> edition: 1404 -1405.
- [11]. Fu YS, Reagan JW. Pathology of the uterine cervix, vagina and vulva. Philadelphia, PA: WB Saunders, 1989.
- [12]. Averette HE, Ford JH Jr, Dudan RC, et al. Staging of cervical cancer. Clin Obstet Gynecol 1975; 18: 215 – 232.
- [13]. Pettersson F. Annual report on the results of treatment in gynecological cancer. Radiumhemmet, Stockholm, Sweden: *International Federation of Gynecology & Obstetrics* (FIGO), 1994: 132 – 168.
- [14]. Smith M, McCartney AJ. Occult, high risk endometrial carcinoma. *Gynecol Oncol* 1985; 22: 154 – 161.
- [15]. MacMohan B. Risk factors for endometrial cancer. *Gynecol Oncol* 1974; 2: 122 – 129.
- [16]. Parazzini F, La Vecchia C, Bocciolone L, et al. The epidemiology of endometrial cancer. Gynecol Oncol 1991; 41; 1 – 16.
- [17]. Podczaski E, Kaminski P, Gurski K, *et al.* Detection and patterns of treatment failure in 300 consecutive cases. *Gynecol Oncol* 1992; 47: 323 – 327.
- [18]. Norris HJ, Roth E, Taylor HB. Mesenchymal tumors of the uterus. II .A clinical pathological study of 31 mixed mesodermal tumors. *Obstet Gynecol* 1996; 28: 57-63.
- [19]. Inthasorn P, Carter J, Valmadre S, *et al.* Analysis of clinicopathogic factors in malignant mixed mulleriantumors of the uterine corpus. Int J Gynecol Cancer 2002; 12: 348 – 353.
- [20]. Taylor HB, Norris HJ. Mesenchymal tumors of the uterus. IV. Diagnosis AND Prognosis of leiomyosarcoma. Arch Pathol 1966; 82: 40 – 44.
- [21]. Czesnin K, Wronkowski Z. Second malignancies of the irradiated area in patients treated for uterine cervix cancer. *Gynaecol Oncol* 1976; 6: 309 315.
- [22]. Salazar OM, Bonfiglio TA, Patten SF, *et al.* Uterine sarcomas: analysis of failures with special emphasis on the use of adjuvant radiation therapy. *Cancer* 1978; 42: 1161 – 1170.
- [23]. Norris HJ, Taylor HB. Melanomas of the vagina. *Am J Clin Pathol* 1966; 46: 420.
- [24]. Ledward RS. Primary carcinoma of the vagina: A review of 21 cases treated at the Samaritan Hospital for Women 1947-70. *Proc R Soc Med.* 1972 Jan; 65(1): 95-7.
- [25]. Benedet JL, Murphy KJ, Fairy RN, et al. Primary invasive carcinoma of the vagina. Obstet Gynecol 1983; 62:715 719..Jones RW, Baranyai J, Stables S. Trends in squamous cell carcinoma of the vulva: Obstetic Gynecol 1997; 90:448 452.