



Epidemiology of Female Genito-Urinary Malignancy

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Abstract: Background: The incidence of endometrial cancer is higher in more developed areas of the world compared to less developed countries, indicating a possible influence of environmental factors on the incidence of this disease. The most common pathological type is endometrioid adenocarcinoma, constitute 75% to 80% of all cases. This study aimed to determine the burden of female genito-urinary malignancy, describe the Clinico-pathological pattern of all female genito-urinary tumors and find tools for screening and early diagnosis. **Methods:** This retrospective study carried out on 362 patients who were histopathological proved to have female genito-urinary malignancies. Patients less than 18 years old, Female patients with second primary rather than genitourinary tract malignancies were excluded from the study. Patients were categorized to patients of genital tract malignancy and of urinary tract malignancy. Patients were subjected to pathological examination, laboratory investigations including (CPC, liver and renal functions and tumour markers) and radiological investigations including (Ultrasound ,chest radiograph , CT/MRI abdomen & pelvis and bone scan). **Results:** Endometrial carcinoma was the most common malignancy found among all studied patients through the period of the study, 115 patients (31.8%) of all studied patients. In bladder cancer patients, 31 patients (55.4%) received 3D conformal radiotherapy, 9 patients (16.1%) received 2D palliative radiotherapy. In uterine cancer patients, 45 patients (39.1%) received 3D conformal radiotherapy, 10 patients (8.7%) received 2D radiotherapy & 2 patients (1.7%) received combined (EBRTH + brachytherapy). The differences were statistically significant ($p > 0.05$). **Conclusions:** As a part of Egyptian state policy to take care of health file in general & women's health particularly, this study was done to register the cases of female genito-urinary malignancy & discuss the possible ways to decrease the burden of that disease and offer the best ways of treatment and early detection.

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1. Introduction:

The national cancer registry program of Egypt (NCRP) published those genitourinary malignancies in females ranks the fourth^[1].

The incidence of endometrial cancer is higher in more developed areas of the world (5.5%) compared to less developed countries (4.2%), indicating a possible influence of environmental factors on the incidence of this disease^[2]. The most common pathological type is endometrioid adenocarcinoma, constitute 75% to 80% of all cases^[3].

Worldwide, cervical cancer remains the most common gynecologic cancer and the fourth most common malignancy in women, with over 526,000 women globally developing this tumor as reported in 2015 and 239,000 dying of the disease every year^[4]. In Egypt, the incidence of cervical cancer is 0.75 %^[5].

In Egypt ovarian cancer ranks the fifth most common malignancy in females it constitutes 4.1 %^[5]. Annual incidence of ovarian cancer per 100,000 of females is 4.5 % in Gharbeya^[1].

Vaginal cancer is considered a rare tumor it represent 0.04% of all female malignancy worldwide^[4].

Vulvar cancer is a rare gynecological malignancy, most commonly affects the outer vaginal lips. Less often, the inner vaginal lips, clitoris, or vaginal glands^[6].

Bladder cancer is less common in females than males it's found in 0.27% of females while found in 1.08% of males worldwide^[4].

There are well-known associations of squamous cell bladder carcinomas with bilharzia caused by *Schistosoma haematobium* infection in Africa, particularly in Egypt Aromatic amines, polycyclic aromatic and chlorinated hydrocarbons arsenic-laced drinking water, aristolochic acid, cyclophosphamide exposure, and a range of industrial chemicals have been implicated in urothelial carcinogenesis. Importantly, as with most carcinogens^[7].

Renal malignancy isn't one of the common malignancy it represent only 3.1% of female malignancies^[4].

This study aimed to determine the burden of female genito-urinary malignancy, describe the Clinico-pathological pattern of all female genito-urinary tumors and find tools for screening and early diagnosis.

2. Patients and Methods:

This retrospective study carried out on 362 patients who were histopathological proved to have female genito-urinary malignancies. Patients less than 18 years old, Female patients with second primary rather than genitourinary tract malignancies were excluded from the study. Our patients were categorized to patients of genital tract malignancy about 277 patients (76.5%) & patients of urinary tract malignancy 85 patients (23.5%).

All patients in this study were subjected to the following:

1-Careful history taking:

Personal history including (age, special habits, and marital status), present history including (patients complain), family history, menstrual history including (contraception and hormonal treatment) and past history.

2- Recorded data of clinical examination:

General examination which includes general appearance, vital signs, head & neck, chest, upper and lower limb examination. Local examination which includes abdomen & pelvic examination.

Investigations:

1-Pathological finding: Pathologically proven to have female genitourinary malignancy.

2-Laboratory investigations: Complete blood count, liver and renal functions and tumour markers eg: CA125 in ovarian cancer patients

3-Radiological investigations: Ultrasound, chest radiograph, CT/MRI abdomen & pelvis and bone scan.

Methods:

- Five-year study involved a review of pathologically proven genitourinary malignancies seen at clinical oncology department Tanta university hospitals from Aug 2014 to Sep 2019.
- Relevant information was gathered from the hospital based registry
- Data extracted from the records included patient age, detailed medical history, sociodemographic profile, organ involved, laterality of the tumor where appropriate, histological characteristics of the tumour, and previous treatment.

D-Privacy:

Privacy of all patients, data is guaranteed and every patient will have a file with a private code number including all investigations.

Statistical analysis

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp), the numerical variables were presented as mean & standard deviation. For categorical variable the number and percentage was calculated, p value for significance was adopted at <0.05. The used tests were Chi-square test: for categorical variables, to compare between different groups and Monte-Carlo Exact (MCET) test: for estimation of the exact significance levels for the statistics available through the cross tables.

3 Results:

Table (1) shows patient characteristics.

Table 1: Patient characteristics (n= 362):

Mean age \pm SD		N	%
	>56 \pm 13.5		203
\leq 56 \pm 13.5		159	43.9
Site of malignancy & Mean age of each	Bladder (Mean age 66)	56	15.5
	Kidney (Mean age 54)	28	7.7
	ureter	0	0
	Urethra (Mean age 57)	1	0.3
	Ovary (Mean age 47)	111	30.7
	Uterus (Mean age 55)	115	31.8
	Cervix (Mean age 51)	43	11.9
Menstrual status	Vulva (Mean age 74)	8	2.2
	Premenopausal	75	20.7
Marital status	Postmenopausal	287	79.3
	Married	304	84
	Single	19	5.2
Parity status	widow	39	10.8
	single parity	70	19.3
	multiparity	194	53.6
	nulliparity	46	12.7
Contraception	unregistered	52	14.4
	hormonal	152	42
	non hormonal	172	47.5
Family history	unregistered	38	10.5
	Positive	40	11
Special habits	Irrelevant	322	89
	Smoking	2	0.6
Comorbidities	Non	360	99.4
	Hypertension	97	26.8
	Diabetes mellitus	29	8
	Cardiac problem	13	3.6
	Combined	49	13.5
	Not present	174	48.1

Table (2) shows the distribution of the studied patients according to Egypt's governorate, in Gharbia governorate by their administrative areas, according to different histopathological patterns and pathological grading & staging during period of study (2014-2019).

Table 2: The distribution of the studied patients according to Egypt's governorate , in Gharbia governorate by their administrative areas , according to different histopathological patterns and pathological grading & staging during period of study (2014-2019)

Governorate	2014		2015		2016		2017		2018		2019	
	N = 49		N = 62		N = 47		N = 98		N = 66		N = 40	
	N	%	N	%	N	%	N	%	N	%	N	%
Gharbia	33	67.3	36	58.1	27	57.4	70	71.4	55	83.3	28	70
Monefia	2	4.2	3	4.8	3	6.4	7	7.2	2	3.1	0	0
Behera	0	0	2	3.2	3	6.4	1	1	3	3.1	2	5
Kafr EL-Sheikh	12	24.5	5	8.2	10	21.3	12	12.2	2	3.1	6	15
Kaliobeia	0	0	0	0	0	0	1	1	0	0	1	2.5
Dakahlia	1	2	1	1.6	2	4.2	2	2	0	0	2	5
Alex, Cairo& Matrouh	0	0	0	0	0	0	0	0	0	0	1	2.5
Unregistered	1	2	15	24.1	2	4.3	5	5.2	4	6.3	0	0
Gharbia governorate												
El Mahalla El Kobra	13	39.4	15	41.6	10	37	16	22.8	26	47.3	13	46.4
Tanta	11	33.3	8	22.2	10	37	17	24.3	12	21.8	7	25
Kafr El-Ziat	4	12.1	3	8.3	3	11.2	12	17.2	5	9.1	3	10.7
El Santa	1	3	6	16.7	2	7.4	6	8.6	2	3.6	2	7.1
Kotor	1	3	2	5.6	0	0	4	5.7	2	3.6	1	3.6
Zefta	0	0	2	5.6	2	7.4	3	4.3	1	1.8	0	0
Bassune	2	6.2	0	0	0	0	7	10	3	5.5	1	3.6
Samanoud	1	3	0	0	0	0	5	7.1	4	7.3	1	3.6
Histopathological pattern												
											N	%
adenocarcinoma											129	35.6
squamous cell carcinoma											52	14.4
Transitional cell carcinoma											48	13.3
Serous cell carcinoma											31	8.6
Clear cell carcinoma											27	7.5
mucinous cell carcinoma											21	5.8
sarcoma											19	5.3
unknown											9	2.5
choriocarcinoma											8	2.2
teratoma											3	0.8
Signet ring carcinoma											3	0.8
carcinosarcoma											3	0.8
granulosa cell tumour											2	0.6
Yolk sac tumour											2	0.6
sertolilydig cell tumour											2	0.6
dysgerminoma											2	0.6
neuro endocrine tumour											1	0.3
Total											362	100
pathological grading & staging												
Grading												
I											52	14.4
II											160	44.2
III											94	26
IV											1	0.3
unknown											55	15.2
Staging												
I											99	27.3
II											126	34.8
III											91	25.1
IV											46	12.7

Table (3) Shows the relationship between tumor site & patient age and different pathological patterns.

Table 3: The relationship between tumour site & patient age and different pathological patterns

Age	Site of tumor														MCET P
	Bladder		Kidney		Urethra		Ovary		Uterus		Cervix		Vulva		
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	
>56 (n=203)	51	25.1	13	6.4	1	0.3	46	22.7	73	36	12	5.9	7	3.4	0.001*
<56 (n=159)	5	3.1	15	9.4	0	0	65	40.9	42	26.4	31	19.5	1	0.6	
Pathology															
	N = 56		N = 28		N = 1		N = 111		N = 115		N = 43		N = 8		
Transitional cell carcinoma	46	82	0	0	0	0	2	1.8	0	0	0	0	0	0	
Squamous cell carcinoma	8	14	0	0	1	100	0	0	0	0	35	81	8	100	
Adenocarcinoma	2	3.6	0	0	0	0	29	26	90	78.3	8	19	0	0	
Clear cell carcinoma	0	0	27	96	0	0	0	0	0	0	0	0	0	0	
Neuroendocrine tumour	0	0	0	0	0	0	0	0	1	0.9	0	0	0	0	
Mucinous cell carcinoma	0	0	0	0	0	0	21	19	0	0	0	0	0	0	
Serous cell carcinoma	0	0	0	0	0	0	31	28	0	0	0	0	0	0	
Sarcoma	0	0	1	3.6	0	0	4	3.6	14	12.2	0	0	0	0	
Signet ring carcinoma	0	0	0	0	0	0	3	2.7	0	0	0	0	0	0	
Teratoma	0	0	0	0	0	0	3	2.7	0	0	0	0	0	0	
Yolk sac tumour	0	0	0	0	0	0	2	1.8	0	0	0	0	0	0	
Dysgerminoma	0	0	0	0	0	0	2	1.8	0	0	0	0	0	0	
Granulosa cell tumour	0	0	0	0	0	0	2	1.8	0	0	0	0	0	0	
Sertoli Leydig cell tumour	0	0	0	0	0	0	1	0.9	0	0	0	0	0	0	
Carcinosarcoma	0	0	0	0	0	0	9	8.1	2	1.7	0	0	0	0	
Choriocarcinoma	0	0	0	0	0	0	0	0	8	7	0	0	0	0	

MCET =Monte Carlo Exact Test, *Statistically significant ($P<0.05$)

Table (4) shows surgical intervention in each tumour site.

Table 4: The surgical intervention in each tumour site

Treatment received	Site of tumour											
	Bladder		Kidney		Ovary		Uterus		Cervix		Vulva	
	N = 56		N = 28		N = 111		N = 115		N = 43		N = 8	
Surgical intervention	N	%	N	%	N	%	N	%	N	%	N	%
TAHBSO	0	0	0	0	58	52.2	104	90.4	25	58.1	0	0
Oophorectomy	0	0	0	0	16	14.4	0	0	0	0	0	0
Ovarian cystectomy	0	0	0	0	4	3.6	0	0	0	0	0	0
Uterine evacuation	0	0	0	0	0	0	3	2.6	0	0	0	0
Pelvic exenteration	0	0	0	0	0	0	0	0	1	2.3	0	0
Vulvectomy	0	0	0	0	0	0	0	0	0	0	5	62.5
Exploration	0	0	0	0	1	0.9	1	1	0	0	0	0
Cystectomy	3	5.4	0	0	0	0	0	0	0	0	0	0
Nephrectomy	0	0	26	92.9	0	0	0	0	0	0	0	0

Table (5) shows The distribution of the studied patients who received radiotherapy and who received cording to its different types.

Table 5: The distribution of the studied patients who received radiotherapy

Treatment received	Site of tumour														MCETP
	Bladder		Kidney		Urethra		Ovary		Uterus		Cervix		Vulva		
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	
Radiotherapy															0.012*
EBRTH (3D)	31	55.4	5	18	1	100	1	0.9	45	39.1	25	58.1	4	50	
EBRTH (2D)	9	16.1	8	28.6	0	0	10	9	10	8.7	7	16.3	1	13	
Brachytherapy	0	0	0	0	0	0	0	0	0	0	1	2.3	0	0	
Combined therapy	0	0	0	0	0	0	0	0	2	1.7	1	2.3	0	0	

MCET = Monte Carlo Exact Test, *Statistically significant ($P < 0.05$)

Table (6) shows The distribution of the studied patients who received chemotherapy according to its different types.

Table 6: The distribution of the studied patients who received chemotherapy according to its different types.

Treatment received	Site of tumour														MCETP
	Bladder		Kidney		Ovary		Uterus		Cervix		Vulva				
	N	%	N	%	N	%	N	%	N	%	N	%			
Chemotherapy															0.027*
Taxines based	6	10.7	0	0	63	56.8	18	15.6	2	4.7	0	0			
Platinum based	9	16.1	1	3.6	6	5.4	3	2.6	0	0	0	0			
Anthracyclin based	0	0	0	0	0	0	3	2.6	0	0	1	12.5			
Single agent gemcitabin	4	7.1	0	0	5	4.5	3	2.6	0	0	0	0			
Single agent platinol	8	14.3	0	0	1	0.9	3	2.6	9	20.9	5	62.5			

MCET = Monte Carlo Exact Test, *Statistically significant ($P < 0.05$)

Table (7) shows relationship between site of primary & site of metastases among studied patients.

Table 7: Relationship between site of primary & site of metastases among studied patients

Site of tumour	Site of metastasis										MCETP
	Bone		Visceral		Both		Non metastatic				
	N	%	N	%	N	%	N	%			
Bladder (n=26)	7	12.5	0	0	0	0	49	87.5	0.048*		
Kidney (n=28)	2	7.1	3	10.7	4	1.1	19	5.2			
Ovary (n=111)	8	16.2	8	16.2	1	0.9	94	84.7			
Uterus (n=115)	6	5.2	3	2.6	2	1.7	104	90.4			
Cervix (n=43)	4	9.3	7	16.3	0	0	32	74.4			
Vulva (n=8)	0	0	0	0	0	0	8	100			

MCET = Monte Carlo Exact Test, *Statistically significant ($P < 0.05$)

4. Discussion

Occurrence of genito-urinary malignancy may be attributed by certain behaviours or risk factors, such as smoking, alcohol intake, junk foods, low fibres diet & some of those malignancies resulted from parasitic or viral infections as bladder and cervical cancers [8].

In our study, the number of bladder cancer patients was 56 (66%), the number of renal cell carcinoma was 28 (32.9%) & the number of the patients with cancer urethra is 1 (1.2%) while there is

no patients of cancer ureter through the period of study, while in Akbari et al. [9] study which studied the incidence of genitourinary tract malignancies in Islamic republic of Iran in 2005 and included 8147 of male & female patients, the number of female patients with bladder cancer was 689 (66.4%), the number of female patients with renal cell carcinoma was 313 (20.3%), while the number of this category of patients of cancer ureter was 21 (2.02%), and the number of female patients of cancer urethra was 10 (0.96%) [9]. As regard to age in our study, the mean age of bladder

cancer patients was 66 years, while in **Moussa & El-Sheshtawy** ^[10] study which studied the pathological pattern in bladder cancer patients in clinical oncology department Al-Azhar university and included 632 patients, the mean age in that study was 58 years ^[10].

In our study, the mean age of renal cancer patients was 54 years while in **Nardi et al** ^[11] study which studied the epidemiologic characteristics of renal cell carcinoma in Brazil and reported 508 patients, the mean age of those patients was 59 years ^[11].

In our study, the most predominant pathological patterns among urinary tract malignancies were transitional cell carcinoma it was found in 48 (56.4%) and this matches with **Klufio et al** ^[12] study, in which the most predominant pattern among urinary tract malignancies was transitional cell carcinoma, it was found in 59 (50.4%) and this may be as bladder cancer was the commonest type of urinary tract ^[12].

As regard to staging in our patients with bladder cancer, it was found that stage II was the most predominant as it was found in 33 (59%) of bladder cancer patients, and this matches with **Rawlings et al** ^[13] study, which studied radiotherapy alone versus concurrent chemo radio in bladder cancer treatment and included 360 patients, in which 297 (82.5%) was stage II ^[13].

In our study, uterine cancer was the highest incidence in genital tract malignancies, it was found in 115 (41.5%), while the number of ovarian cancer patients was 111 (40%), the number of cervical cancer patients was 43 (15.5%) & patients with cancer vulva was 8 (3%), in contrary with **Pankaj et al** ^[14] study which studied the surgically treated gynecologic malignancies at the tertiary care center in Bihar, India and included 264 cases of gynecological malignancies, the number of ovarian cancer patients was 150 (56.8%), while the number of uterine, cervical & vulval cancer patients was 26 (9.8%), 83 (31.4%) & 3 (1.14%) respectively ^[14].

In our study, adenocarcinoma was the most predominant histopathological pattern in female genital tract malignancies about 129 (46.5%) and this as the uterine cancer is the most common cancer in our study, while in **Pankaj et al** ^[14] study, serous cystadenocarcinoma was the most predominant histopathological patterns about 91 (28.4%) and this as the ovarian cancer is the most common gynecological malignancy in this study ^[14]. As regard to stage in our study, stage I was the most predominant one among the patients of genital tract malignancies, it was found in 84 (30.3%) and this matches with **Yamagami et al** study, which studied the clinical statistics of gynecologic cancer in Japan and this may be due to use of screening tools for early

detection and treatment of gynecological malignancies & the high patient awareness in this country ^[15].

While stage IIA -IIIB was the most predominant in patients of **Pankaj et al** ^[14] study, it was found in 91 (34.5%) ^[14].

As regard to radiotherapy in cervical cancer patients in our study, 34 (79.1%) of them received radiotherapy, and this matches with **Shrivastava S, et al** ^[16] study in which 675 (71%) of cervical cancer patients received radiotherapy ^[16]. In our study, metastatic patterns of ovarian cancer patients were equal in both bone & viscera and this matches with **Lengyel, et al** ^[17] study, which studied ovarian cancer development and metastasis, in which the ovarian cancer metastases were equal in both bone & viscera ^[17].

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