

Prevalence of Different Types of Genitourinary Tract Malignancies Presenting to the Histopathology Departments of Al-Thawra Hospital over a period of 5 years

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Abstract

Background: Cancer is the public health problem. The burden of cancer is increasing worldwide despite the advances for diagnosis and treatment. **Aim:** To analyze the genitourinary tract malignancies presented to histopathology department in TGMH over a period of 5 years. **Methods:** A descriptive hospital based study was conducted at the histopathology departments in TGMEH, Sana'a/Yemen from January 2006 to December 2010. All the consecutive GUT specimens presenting for histopathology were included in the study. **Results:** The total number of specimens dealt with during this period was (11071) out of which 4.5% (499) were GUT malignant tumors. The peak age for presentation was between 0.6-95 (Mean 56.1) in males, while it was 1-85 (Mean 46.7) in females. In males the top five GUT malignant tumors involved the transitional cell cancer 157 (31.3%), prostate Adenocarcinoma 84 (16.8%), Squamous cell cancer 52 (10.4%), Renal cell cancer 25 (5.0%) and Wilm's Tumor 13 (2.6%). Among females the most frequently seen urological tumors were Renal cell cancer 44 (8.8%), Transitional cell cancer 42 (8.4%), Squamous cell cancer 28 (5.6%) and Wilm's tumor 17 (3.4%). **Conclusion:** The most common GUT in male is transitional cell cancer of the urinary bladder and in female the renal cell cancer. The mean age of urinary bladder and renal cell cancer is approximately a decade younger than Western patients. Schistosomiasis remains an important health problem in Yemen.

Key Words: Schistosomiasis, GUT, Malignant tumors, Sana'a

Introduction:

The burden of cancer is increasing worldwide despite the advances for diagnosis and treatment. It is estimated that in the year 2008 worldwide 12.4 million new cases of cancer were reported and 7.6 million people died¹. According to the National Vital Statistics Report malignancies were the second most common cause of death in USA in 2006². The estimations from Europe are that 3.2 million new cases and 1.7 million deaths from cancer were seen in 2008³. It is predicted that by 2030 there will be approximately 20 million new cases and 12.9

million deaths related to cancer. In the United States 2009, an estimated 333,000 people were diagnosed with genitourinary cancers, and approximately 56,000 died of these diseases. The American Cancer Society estimates that genitourinary cancers accounted for 23 percent of all new cancer diagnoses and approximately 10 percent of all cancer deaths in 2009⁴.

The incidence of cancer is steadily increasing in the underdeveloped countries. More than half of the new cases and around 60% of the cancer related deaths occurred in these countries. The causes for cancers can be either

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internal factors like inherited mutations, hormones, and immune conditions or environmental factors such as tobacco, diet, radiation, or other infectious agents⁵.

There are marked differences in distribution of different cancers in different regions of the world⁵. In Kingdom of Saudi Arabia, Genitourinary cancer accounts for only 9.2% of all cancers, while the rate in the United States of America (USA) is as high as 24.1%. The most common genitourinary cancer in Saudi is bladder, followed by the prostate, kidney, and testicular cancer ⁶.

The republic of Yemen lacks a national cancer registry and there are no reliable data available⁷. There are only few, published studies of the pattern of cancers or some malignancies in some parts of the Republic of Yemen⁷⁻¹⁶. Many studies conducted in Yemen revealed that the most common type of cancer was gastrointestinal tract malignancies followed by lymph node cancer and head and neck malignant tumors^{7,8}. Sana'a is the most populous of all provinces of Yemen and the largest city with an estimated population approaching 2 million ¹⁷.

Aim of the study: To analyze the genitourinary tract malignancies presented to histopathology department in TGMH over a period of 5 years.

Subjects and Methods

This descriptive, hospital based study was carried out in Sana'a City, Yemen. All specimens were collected from the histopathology department and fixed in bloc in formalin and submitted for histological assessment. The study included all GUT malignant cases diagnosed from January 2006 to December 2010. The tissue was processed in a tissue processor and paraffin blocks were made. The slides were examined by a consultant, who is one of authors and the results were recorded.

The patient's name, sex, age, diagnosis and site of tumor were fed into computerized data sheet (SPSS), and a numerical code was given for each source. Pediatric GUT malignancies were separated (< 15 years), according to site of cancer. The neoplasm's were arranged at first according to the main topographic classification of tumors

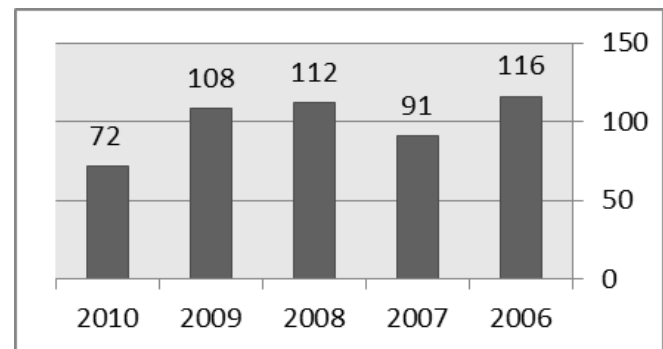
and then rearranged by using sub-classification to specify the most affected site in both males and females. The Statistical Package for Social Science (SPSS, version 11.0) analyzed the result. Result were expressed as means, and standard deviations (SD) and the significance was analyzed by independent t-test to compare the groups and paired t-test was used to analyze the significance in the inter group. The significant different was indicated if p-value <0.05. The results of our study were compared with other local, regional and international studies.

Results

The total number of specimens dealt with during five years period was (11071) out of which 499 (4.5%) were genitourinary tract malignant tumors.

Figure 1 shows no increase in overall prevalence of GUT malignant tumor observed in the period from 2006-2010 and the slight decrease in number of cases in (2010) is a result of the political situation (doctors union upset).

Figure 1: Cases distribution, Sana'a, 2006-2010



The male tumors were in 360 cases (72.1%) and the female 139 cases (27.9%). Adults comprised 92.8% and children 7.2 %.The organ specific frequency of occurrence is shown in Table 1.

According to the sites of occurrence the Urinary bladder cancer is the most frequent, it accounts for 291 (58.3%) of the GUT diagnosed cancer and comprised 2.63 % of total cancer cases in Sana'a. The second most frequent is the kidney tumor it constitutes 109 (21.8%). Prostate malignancy occurred in 86 cases (17.2%) and is the third most frequently cancer, it accounts for 24% of all male cancer. Scrotal tumors is not very common, it constitutes

13(2.6%) of all GUT malignancies and only 3% of total male GUT malignant tumor. Table 1. The peak age for occurrence was between 0.6-95 (Mean 56.2, SD 17.68) in males, while it was 1-85 (Mean: 46.6, SD: 20.26) in females. Figure 2.

This difference in mean ages was found ($P < 0.001$).

Table 1: Genitourinary cancers, Sana'a 2006-2010

Variables	F	%	Mean	SD
Valid Urinary Bladder	291	58.3	56.237	13.2
Renal Tumor	109	21.8	37.562	24.8
Scrotal Tumor	13	2.6	33.462	15.2
Prostate	86	17.2	67.395	9.1
Total	499	100	53.538	18.9

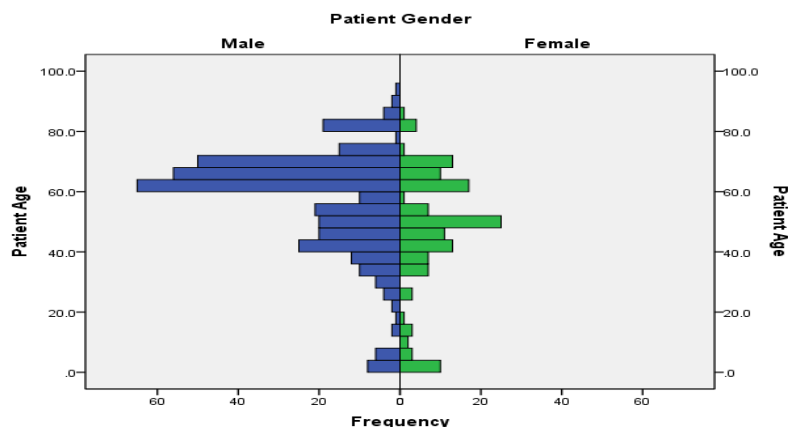
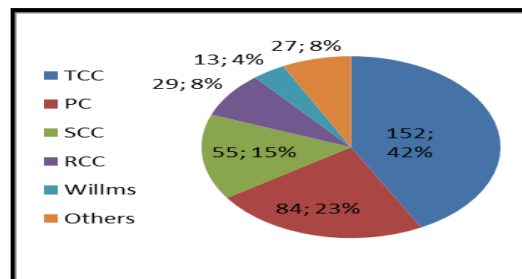


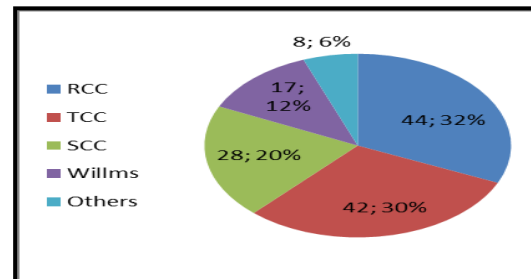
Figure 2: Age distribution of GUT cancers in male and female, Sana'a, 2006-2010.

In males the top five GUT malignant tumors involved the transitional cell cancer 152 (42%), prostate Adenocarcinoma 84 (23%), Squamous cell cancer 55 (15%), Renal cell cancer 29 (8%) and Wilm's Tumor 13 (4%). Among females the most frequently seen urological tumors were Renal cell cancer 44 (32%), Transitional cell cancer 42 (30%), Squamous cell cancer 28 (20%) and Wilm's tumor 17 (12%). Figure 3.

Figure 3: Distribution of GUT cancers by sex, Sana'a, 2006-10.



Male



Female

Transitional cell cancer (TCC), Prostate Adenocarcinoma (PC), Squamous cell cancer (SCC), Renal cell cancer (RCC), Wilm's Tumor

Table 2: Distribution of GUT cancers according to sex and age

Cancer site	Cases	%	Ratio	Mean Age (Year)	Rang (Year)	±SD
Urinary bladder cancer						
Male	214	74	2.78:1			
Female	77	26				
Transitional cell cancer						
Male	152	77	3.38:1	58.26	26 – 95	14.07
Female	45	23		57.15	35 – 80	11.60
Squamous cell cancer						
Male	55	66	1.96:1	50.56	25 – 70	12.07
Female	28	34		48.65	35 – 70	10.25
Others*						
Male	8	72.7				
Female	3	27.3				
Kidney malignancy						
Male	46	42	0.7:1			
Female	63	58				
Adults						
Renal cell cancer						
Male	29	40	0.66:1	57.3076	35 - 85	12.46
Female	44	60		48.1385	17 - 85	14.47
Children						
Wilm's tumor						
Male	13	43	076:1	4.7999	0.5 - 12	2.88
Female	17	57		3.7769	1 - 15	4.42
Prostate						
Prostate Adenocarcinoma	84	98		67.750	38 - 90	8.38
Transitional cell cancer	2	2				
Testis	13	100		33.462	16-65	15.24

Others*: Adenocarcinoma, Undifferentiated cancer, Rhabdomyosarcoma

The mean ages of the transitional cell cancer (TCC) cases of the urinary bladder are statistically approximate in both genders ($p=0.08$) as well as in squamous cell carcinoma (SCC), but the comparison of mean age in both gender between the two malignancies is found significant different of about a decade.

A comparison is made between patients with TCC and those with SCC in table 2. In this series, the mean age of

patients with SCC (50.6 years) was significantly less than those with TCC (58.3 years).

The male to female ratio of cases with TCC (3.38:1) are significantly higher than those with SCC (1.96:1).

Low grade non-muscle invasive TCC present in 123 cases and the remainder present as high grade cancer.

All squamous cell carcinomas were muscle infiltrating at the time of diagnosis, while 62% of transitional cell carcinomas were superficial.

About 52 % have SCC that invaded into deeper layers but still contained in the urinary bladder. In 46% of cases, the cancer spread to the nearby tissues of urinary bladder. Rarely (2% of SCC cases), it has spread to distant sites.

In comparing the cell differentiation in, the high grade TCC comprises 38% while in high grade SCC it comprises 65%, this differences was statistically significant.

The comparison of the renal cell cancer mean ages to the gender shows about 10 years difference. It occurs in female younger than those seen in male and this age difference was statistically significant ($P<0.001$).

Table 3: Histological classification of urinary bladder and kidney malignancies by sex.

Cancer site	Histological types	Sex (%)				Total	
		Male		Female		n	(%)
Urinary bladder	Transitional cell cancer	152	52	45	16	197	68
	Squamous cell cancer	55	20	28	10	83	28
	Adenocarcinoma	4	1	1		5	2
	Undifferentiated cancer	3	1	2		5	2
	Rhabdomyosarcoma	1		0		1	
Total		215	74	76	26	291	100
Kidney	Renal cell cancer	29	27	44	40	73	67
	Wilm's tumor	13	12	17	16	30	27
	Transitional cell cancer	1	1	1	1	2	2
	Squamous cell cancer	1	1	0	0	1	1
	Adenocarcinoma	1	1	0	0	1	1
	Oncocytoma	0	0	1	1	1	1
	Non-Hodgkin lymphoma	1	1	0	0	1	1

The peak age of the prostate Adenocarcinoma was between 60-70 Years (74% of all cases). In this peak age the prostate Adenocarcinoma in comparing with the other genitourinary cancers comes in the first place ($P<0.001$).

The prostate Adenocarcinoma in 51.6% of the cases are well to moderately differentiated. Figure 4.

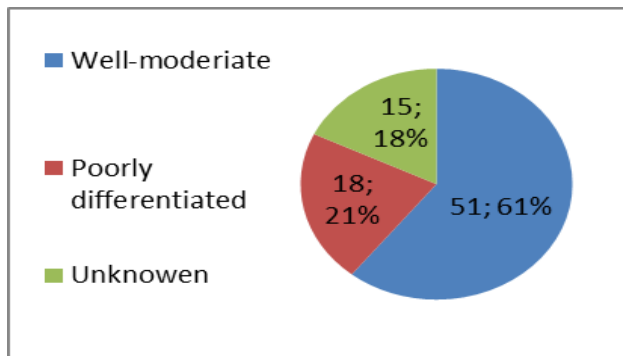


Figure 4: the cell differentiation of prostate Adenocarcinoma.

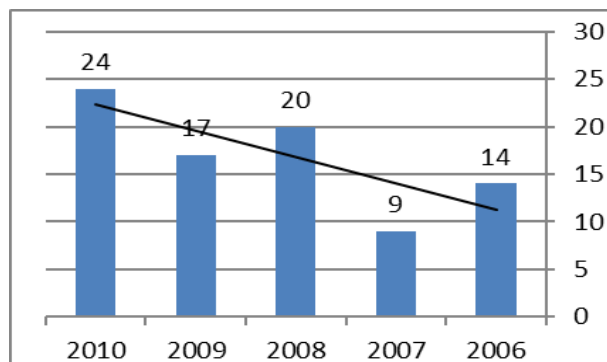


Figure 5: distribution of Prostate Adenocarcinoma , Sana'a, and 2006-2010

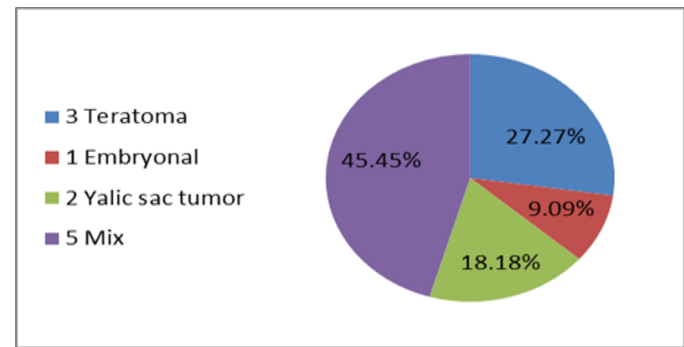
Eggs of schistosomiasis haematobium were seen in microscopic section of the urinary bladder tumor in 29% of patients with squamous cell carcinoma and in 4% of the patients with transitional cell cancer. This difference of associated schistosomiasis eggs with SCC was statically significant. Table 4.

Table 4: Schistosomiasis associated urinary bladder cancer (SABC).

Histology	SABC	Not seen	Total
Squamous cell cancer	24 (29%)	59	83
Transitional cell cancer	7 (4%)	190	197

The testicular tumor (13 Cases) classified into Seminoma and Non- seminoma. The Seminoma occur in 2 cases (15%) and the non-seminoma in 11 cases (85%). Figure 6.

Figure 6: histological distribution of the non-seminoma cases (2006-2010)



Discussion

The Republic of Yemen lacks a national cancer registry and exact date to support the clinical impression that the incidence rate increased has not been available. We can only guess the prevalence rate of the various cancers according to the hospital based registry. Information regarding the relative frequency of different tumors can be obtained from sources such as the pathology department. However, if we consider the WHO recommendation for estimating cancer incidence (100 per 100000 for countries with more than half of the population under 20 years of age), the number of new cases in Yemen should be around 16000 annually⁷. The subject of genitourinary cancer in the elderly population in USA becomes increasingly more important. Carcinoma of the kidney, bladder, and prostate all have an increasing incidence over the age of 50 and have a predilection for affecting men more commonly than women¹⁸.

In USA the Genitourinary malignancy comprises nearly half of the cancers diagnosed in men, and the incidence of this group of cancers increases with age¹⁹.

In the present study the GUT malignancy for the five years period constituted 4.5% of all new cancer diagnoses. The pattern in overall prevalence of the GUT cancer was similar and the slight decrease in patients cases in 2010 as a result of political situation in Yemen.

This finding is compared with previous investigations of the pattern of malignancy in Sana'a, which constitute the

GUT malignancy the 5th most common malignancy in Yemen, but they are less common in other studies in South-Eastern governorates of Yemen and province of Hadhramout, which constituted it as the 8th common organ site 8,7,16, 20.

The most common site of cancer within the GUT is the bladder. Urinary bladder cancer comprises 58.3% of genitourinary malignancies and the males are more frequently affected than females (Ratio= 2.8:1), this is similar to others studies 8, 18, 20.

Worldwide, the male-to-female ratio in the incidence of bladder cancer is 3.3:1. However, this ratio varies around the world and has been reported as 1.1:1.0 in Eastern Africa, 2.1:1.0 in South Africa, 5:1 in Northern Africa and 5.1:1.0 in several areas of southern Europe 5,21. In some countries this ratio was higher, 10.4 for Denmark, 9.6 for Iceland, 8.6 for the UK, 7.4 for Jordan, 6.9 for Israel (Arabs) and 5.3 for Cyprus 22-24.

An estimated 386,300 new cases of bladder cancer occurred in 2008, making it the ninth most common cause of cancer worldwide, and there is a 15-fold variation in incidence rates internationally. The highest incidence rates are found in Europe, Northern Africa, and the Middle East, as well as North America. The lowest rates are found in Southeast Asia and Middle Africa 25.

In Europe, cancer of the urinary bladder is the fourth most frequent cancer among men and accounting for about 7% of the total cancers. The annual incidence rate is 22/100,000 in men and 4/100,000 in women and 70% of patients with more than 65 years of age 22.

In Yemen, Bladder cancer is the fourth most commonly diagnosed cancer among men and is the first among the urologic cancers in males and the second organ site in female 8.

The incidence of Urinary bladder Cancer for neighbor countries varieties from high incidence rates present in Egypt 27.9, 18.1 in Israel Arabs, 14.7 in Bahrain, 13.2 in Jordan, but not in Kuwait (6.3), in Oman (5.1), in Saudi (2.5) and in Qatar 1,8, while the incidence in female range

from 3.8 in Bahrain, 3.1 in Egypt to 2.9 in Kuwait, 2,2 in Oman, 1.2 in Saudi and 0.7 in Qatar. This is pointing to considerable variation in risk factors across the Arab world.

The histological pattern of urinary bladder cancer are TCC 68 % and SCC 28% of 291 urinary bladder cancers seen in 5-years period. Rare pathological subtypes of urinary bladder cancer include Adenocarcinoma (2%), undifferentiated cancer (2%) and Rhabdomyosarcoma.

TCC is the most common urinary bladder cancers worldwide, with the highest incidence in Europe and the lowest incidence rates were reported from Asia (China) and South America. Histology data available from North America, Europe and Australia where 92-99% of bladder cancers were TCC as it is expected; whereas the proportion is around 70- 80% in Southeast Asia, and substantially less than 50% in different parts of Africa 26, 27.

The most frequent cases of the TCC are well differentiated cancer and is observed 62%, which usually appears as papillary and superficial lesions, while the SCC are highly malignant and tend to be of high grade at the diagnosis, which frequently presents as a nodular and invasive, 65 % of cases are poorly differentiated lesions. This finding is in agreement with other reports 26-28. Fewer than 2% of these cancers are undifferentiated, aggressive and metastatic.

The proportion of SCC varied from 50 to 81% of all bladder cancer cases in different areas of endemic schistosoma infection in some Middle Eastern and African countries, which contrasts to Western countries, where the frequency of SCC in bladder cancer cases is much lower about 3 to 10% 29, 30.

Traditionally, Schistosoma haematobium has been considered the most important etiological agent 31, but transitional cell carcinoma has recently become the most frequent type in Egypt, replacing lesions with squamous features, corroborating findings from small-scale hospital-

based studies indicating that the etiology of bladder cancer has changed significantly over the past 26 years³².

This lower frequency of SCC relative to previous reports supports the etiological relationship to urinary Schistosomiasis in Egypt and the effect of successful control measures of the endemic disease. The increase in frequency of TCC and decrease in frequency of SCC relative to previous reports indicate a transition phase from the schistosoma-associated bladder carcinoma (SABC) to the Western type of bladder cancer related to smoking³². Cigarette smoking is the most important risk factor, accounting for 50% of cases in men and 35% in women³³. In fact, cigarette smokers have a 2- to 4-fold increased risk of bladder cancer compared to non-smokers³⁴, and the risk increases with increasing intensity and/or duration of smoking³⁵. In Yemen public education, elimination of the parasite by snail control and mass therapy of infected populations will help cancer prevention in the future^{36,37}. This might also explain the low prevalence of SABC in the present result.

In *S. haematobium* associated areas *Schistosoma* eggs are found more frequently in association with squamous cell than transitional cell cancers³⁸.

In the present series eggs of schistosomiasis *haematobium* are seen in microscopic section of the urinary bladder tumor in 29% of patients with SCC and in 4% of the patients with TCC. Other report 28% of patients with bladder tumors in general and 83% with SCC had evidence of urinary schistosomiasis. The high frequency of SCC in schistosomal patients is related to squamous metaplasia and dysplasia, which are common in these patients. Michaud, 2007³⁹ found that transitional cell carcinomas were slightly more common among patients with low schistosoma infection rates (56%), and squamous cell carcinomas were slightly more common (58%) among patients with moderate-to-high levels of infection.

In schistosoma-free countries throughout the world, the peak incidence of bladder cancer is in the sixth or seventh decade of life⁴⁰. Only 12% of bladder cancer cases occur

in people younger than 50 years³⁰. In contrast, in Egypt, Sudan, Iraq, Zambia, Malawi, and Zimbabwe, the mean peak age of bilharzial bladder cancer is between 40 and 49 years^{30,41}.

The majority of patients we saw were below 50 years of age. This age distribution is unlike the data from the West, but in conformity with other series from Saudi Arabia and the Middle East⁴². In our result, the mean age at diagnosis of urinary bladder is 48 years for SCC and 58 years for TCC, about 10 years younger in comparison with other reports^{7,8,30,40}.

This relatively low mean age of Yemeni patients, has serious public health implications due to the loss of productive years of life due to bladder cancer.

Prostate cancer incidence and mortality rate vary widely according to geography and race, with more than 90 fold differences in frequency between highest and lowest⁴³. Prostate Adenocarcinoma is the second most common urogenital malignancy in Yemeni males but the incidence, like other Arabian Gulf and Asian countries (Range from 20 in Israel Arab to 3 in Qatar), is very low compared to Western (25-35% all new cancer in USA) despite the high intake of calories and high consumption of animal fat⁴⁴, 7, 45, 46, 47,48. The prostate adenocarcinoma developed at older ages (67-75 years) similar to the worldwide patterns^{42,44,47}. There is a significant increase in the cases of prostate cancer from 2006 (14 cases) to 2010 (24 cases). This can be related to an increase use of screening programs, better awareness of prostate cancer, improve of the health service and the natural aging of the Yemeni population. Prostatic carcinoma constituted 75% of all male genital cancers seen in men older than 60-70 years.

Kidney cancer is the first most commonly diagnosed cancer in urinary tract among Yemeni female and third most common cancer in male. Renal cell cancer (RCC) comprises the most common kidney malignancy in Yemeni adults and Wilm's tumor in cases under 15 years of age. Other cancer like TCC, SCC, Collecting duct cancer, Oncocytoma and non-Hodgkin lymphoma are rare.

The kidney malignancy in Yemeni females is more frequent (male to female Ratio 0.7-1) in contrast to male in early ages. This needs more future investigations to know the reason for this early occurrence of kidney malignancy in females. Internationally this malignancy constitutes about 3% of all adult cases, common in men twice as in women. The mean ages of the RCC cancer in female (48.14 years St. rd 14.47) at the diagnosis is 10 years younger than the male (57.31 years St. rd 12.46) and this shows a two decades younger than that in United States (USA) and Europe (6th and 7th decade of life). In USA cancer is predominant in old age, 58% of all new cancer cases and 66% of all cancer death occur over 65 years of age 49.

The estimated incidence for the kidney cancer in Arabic countries is a mixture from 5.8 in Kuwait, 4.7 in Bahrain, 4.4 in Israel Arabs, 3.4 in Jordan to 2.5 in Egypt and range from 1.7 to 1.6 in Saudi, Omani and Qatar respectively.

Scrotal tumors is less common than other genitourinary cancers, it constitutes 2.6% (13 cases) of all urinary tract malignancies diagnosed in five years period and only 3% of total male urinary tract malignant tumor.

An interesting fact is that in the period of five years there was not a single case of penile carcinoma recorded.

This study of urinary tract malignancy is the first of its type in Yemen, and we plan to study the changes in prevalence of cancer among the Yemeni population in the next five years.

Conclusion

The most common type of cancers found in our study is the TCC of the urinary bladder in male and the RCC is in females while in children under 15 years of age is the Wilm's Tumor more frequent in this age group.

The mean age at presentation of patients was at least 20 years younger than that of develop countries but similar to that of developing countries. No increase in overall prevalence of urinary tract cancer was observed for the period from 2006-2010 and the slight increase in number of prostate cases can be a result of natural aging of the

population. There is the need to set up a population based tumor registry on a national level to calculate the true incidence.

References

1. Boyle, P. and Levin, B. (2008), World Cancer Report 2008, IARC, Lyon: International Agency for Research on Cancer p9.
2. Heron MP, Hoyert DL, Xu J, Scott C, Tejada-Vera B. Deaths: Preliminary data for 2006. National vital statistics reports; vol 56 no 16. Hyattsville, MD: National Center for Health Statistics. 2008. Available from: http://www.cdc.gov/nchs/data/nvsr/nvsr56/nvsr56_16.pdf.
3. Ferlay J, Parkin DM, Steliarova-Foucher E. Estimates of cancer incidence and mortality in Europe in 2008. Eur J Cancer. 2010 Mar; 46(4):765-81. doi: 10.1016/j.ejca.2009.12.014. Epub 2010 Jan 29. PubMed PMID: 20116997.
4. Jemal A, Siegel R, Ward E, Hao Y, Xu J, Murray T, Thun MJ. Cancer statistics, 2008. CA Cancer J Clin. 2008 Mar-Apr; 58(2):71-96. doi: 10.3322/CA.2007.0010. Epub 2008 Feb 20. PubMed PMID: 18287387.
5. Imran Ali, Waseem A. Wani and Kishwar Saleem: Cancer Scenario in India with Future Perspectives. Cancer Therapy 2011, Vol 8, 56-70,.
6. Abomelha MS. Genito-urinary cancer in Saudi Arabia. Saudi Med J. 2004;25(5):552-6. PubMed PMID: 15138519.
7. Bawazir AA, Abdul-Hamid G, Morales E. Available data on cancer in the southeastern governorates of Yemen. East Mediterr Health J 1998; 4: 107-13.
8. AL-Thobhani AK, Raja, a YA, Noman TA. The pattern and distribution of malignant neoplasms among Yemeni patients. Saudi Med J 2001; 22: 910-3.
9. Abdul Hamid G, Tayeb MS, Bawazir AA. Breast cancer in south-east Republic of Yemen. East Mediterr Health J, 2001, 7.1012-6.
10. Abdulmughni YA, Al-Hureibi MA, Al-Hureibi KA, et al Thyroid cancer in Yemen. Saudi Med J, 2004 25, 55-9.

11. Ali AA, Al-Sharabi AK, Aguirre JM, Nahas R A study of 342 oral keratotic white lesions induced by qat chewing among 2500 Yemeni. *J Oral Pathol Med*, 2004. 33, 368-72.
12. Gunaid AA, Sumairi AA, Shidrawi RG, et al. Oesophageal and gastric carcinoma in the Republic of Yemen. *Br J Cancer*, 1995, 71, 409-10.
13. Nasr AH, Khatri ML. Head and neck squamous cell carcinoma in Hajjah, Yemen. *Saudi Med J*, 2000, 21, 565-8.
14. Sawair FA, Al-Mutwakel A, Al-Eryani K, et al. High relative frequency of oral squamous cell carcinoma in Yemen: qat and tobacco chewing as its aetiological background. *Int J Environ Health Res*, 2007, 17, 185-95.
15. Scheifele C, Nassar A, Reichart PA Prevalence of oral cancer and potentially malignant lesions among shammah users in Yemen. *Oral Oncol*, 2007. 43, 42-50.
16. Ghouth AS, Bafageer SS. The pattern and distribution of malignancies reported in Hadramout, Yemen--2006. *J Pak Med Assoc*. 2009 Nov;59(11):774-8. PubMed PMID: 20361678.
17. Ministry of public health and population in Republic of Yemen: <http://www.mophp-ye.org/english/data.html>
18. Mulholland SG, Stefanelli JL. Genitourinary cancer in the elderly. *Am J Kidney Dis*. 1990 Oct;16(4):324-8. Review. PubMed PMID: 2220779.
19. Raghavan D, Skinner E. Genitourinary cancer in the elderly. *Semin Oncol*. 2004 Apr;31(2):249-63. Review. PubMed PMID: 15112154.
20. Ahmed Badheeb – Abubakir Baamer: The pattern and distribution of malignancies reported in Hadramout Sector, Yemen – 2002-2011. *Alandalus For Social and Applied Sciences* 2012, Vol. (5) Issue(8)
21. Yavari P, Sadrolhefazi B, Mohagheghi MA, et al A descriptive retrospective study of bladder cancer at a hospital in Iran (1973-2003). *Asian Pac J Cancer* 2009, Preval, 10, 681-4
22. Ferlay, J, P Boyle. Estimates of cancer incidence and mortality in Europe in 2006. *Annals of Oncology*, 2007
23. Ferlay, J F. Bray, P. Pisani and D.M. Parkin. GLOBOCAN 2002 Cancer Incidence, Mortality and Prevalence Worldwide IARC CancerBase 2004, No. 5, version 2.0 IARC Press, Lyon,
24. Ibrahim AS, Khaled HM Urinary Bladder Cancer. In 'Cancer Incidence in Four Member Countries (Cyprus, Egypt, Israel, and Jordan) of the Middle East Cancer Consortium (MECC) compared with US SEER' Freedman LS, Edwards BK, Ries LAG, Young JL (eds). National Cancer Institute. 2005, NIH Pub. No. 06-5873. Bethesda, MD
25. Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. *Int J Cancer*. 2010 Dec 15;127(12):2893-917. doi: 10.1002/ijc.25516. PubMed PMID: 21351269.
26. el-Mawla NG, el-Bolkainy MN, Khaled HM Bladder cancer in Africa: update. *Semin Oncol*, 2001, 28, 174-8.
27. Scelo G, Brennan P. The epidemiology of bladder and kidney cancer. *Natural Clinical Practice Urol*, 2007, Apr; 4, 205-17.
28. Groeneveld AE, Marszalek WW, Heyns CF. Bladder cancer in various population groups in the greater Durban area of KwaZulu-Natal, South Africa. *Br J Urol*, 1996, 78, 205-8.
29. Parkin DM. The global health burden of infection-associated cancers in the year 2002. *Int J Cancer*. 2006;118:3030-3044.
30. Mostafa MH, Sheweita SA, O'Connor PJ. Relationship between Schistosomiasis and bladder cancer,
31. Bedwani, R., Renganathan, E., El Kwhsky, F., Braga, C., et al.. Schistosomiasis and the risk of bladder cancer in Alexandria, Egypt. *British Journal of Cancer*, 1998, 77(7), 1186-1189.
- Clinical Microbiology Reviews, 1999, 97-111.
32. Felix AS, Soliman AS, Khaled H, et al. The changing patterns of bladder cancer in Egypt over the past 26 years. *Cancer Causes Control*, 2008, 19, 421-9.

- 33.Zeegers MP, Tan FE, Dorant E, van Den Brandt PA. The impact of characteristics of cigarette smoking on urinary tract cancer risk: a meta-analysis of epidemiologic studies. *Cancer* 2000; 89:630–9.
- 34.Kirkali Z, Chan T, Manoharan M, et al. Bladder cancer: epidemiology, staging and grading, and diagnosis. *Urology* 2005; 66:4–34.
- 35.Silverman DT, Devesa SS, Moore LE, et al. Bladder cancer. In: Schottenfeld D, Fraumeni J, editors. *Cancer epidemiology and prevention*, 3rd ed.. New York, New York: Oxford University Press; 2006.
- 36.Nagi MAM.Schistosomiasis and endemic disease control project. Report of the national Schistosomiasis and endemic disease control programme. Sana'a Yemen. Ministry of public health, 2001(YEM/CTD/030): 1-12.
- 37.Nagi MAM.Evaluation of a program for control of Schistosomiasis Haematobium infection in Yemen.YMHRJ/ 2006, November (81-69).
- 38.Tomatis L. Cancer, causes, occurrence and control. Lyon: IARC Press. Pubbl. no. 100. 1990. [Medline]
- 39.Michaud DS (2007). Chronic inflammation and bladder cancer. *Urol Oncol*, 2006, 25: 260–268. doi:10.1016/j.urolonc..10.002 PMID:17483025.
- 40.La Vecchia C, Negri E, D'Avanzo B, Savoldelli R, Franceschi S. Genital and urinary tract diseases and bladder cancer. *Cancer Res* 1991;51(2):629-31.
- 41.Lucas SB. Squamous cell carcinoma of the bladder and schistosomiasis. *East Afr Med J* 1982;59(5):345-51.
- 42.Akhtar SS, Reyes LM. Cancer in Al-Qassim, Saudi Arabia: A retrospective study (1987-1995). *Ann Saudi Med*. 1997 Nov;17(6):595-600. PubMed PMID: 17338003.
- 43.Kym Hickey, Kim Anh Do , and Adele Green .Smoking and Prostate Cancer Epidemiologic review 2001; 23.1: 115-12.
- 44.Mosli HA. Prostate cancer in Saudi Arabia in 2002. *Saudi Med J*, 24, 573-81. Muir CS, Waterhouse J, Mack T, Powell J, Whelan SL (Eds) *Cancer Incidence in Five Continents Vol. V. IARC Scientific Publications* .2003, No 88. 1987 IARC, Lyon.
- 45.Jam al S , Mogh al S , Mamon N, Mushtaq S ,Luqman M, Anwar M . The pattern of malignant tumors: tumor registry data analysis, AFIP, Rawalpindi, Pakistan (1992- 2001). *J Pak Med Assoc* 2006; 56: 359 -62.
- 46.Ghafoor M , Schuyent R , Bener A. Epidemiology of prostate cancer in United Arab Emirates . *Med J Malaysia* 2003; 58: 712 -6.
- 47.Kehinde, E. O., A. O. Akanji, O. A. Mjoimini, A. A. Bashir, et al.. Putative role of serum insulin-like growth factor-1(IGF-1) andIGF binding protein -3 (IGFBP-3) levels in the development of prostate cancer in Arab men. *Prostate cancer and prostatic diseases* 2005, 8(1) 84-96
- 48.<http://en.Wikipedia.org/Wiki/prostate-cancer>.
- 49.American Cancer Society: *Cancer Facts & Figures* 2009. Atlanta, GA; American Cancer Society: 2009