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RESEARCH ARTICLE

RENAL LESIONS: DIFFERENTIATION OF MALIGNANT AND BENIGN TUMORS, SEX AND AGE DISTRIBUTION AND VARIABLES ASSOCIATED WITH RENAL CELL CARCINOMA IN SANA'A CITY, YEMEN

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ABSTRACT

Background: In Yemen there are only a few special epidemiological studies dedicated to malignancy, and for this motivation it is necessary to strengthen, update, construct and continue to afford studies on tumor comportments with the plan of achieving better influence on public health, with early diagnosis and suitable treatment with the plan of enhance survival of living and reducing the feasible subsequent consequences of malignancy.

Aims: The study designed to illustrate the different types of kidney cancer (KC), the gender and age distribution of the cancer, and to identify the different types of them and their correlation with invasion and gradation; and its association with age groups and gender.

Subjects and methods: A retrospective observational study was performed on renal masses patients who were consequently diagnosed selectively by histopathological study in the National Center for Public Health Laboratories (NCPHL) at the Department of Pathology, and the Department of Pathology in Al-Thorah university hospital, Sana'a, Yemen, over a period of 18 years from January 1, 2004 to December 31, 2021. Data were collected from hospital records. The study variables were lesions histological types, benign, malignancy, non-neoplastic lesions**,** sex, grades and age. The whole data were analyzed by IBM SPSS Statistics 22.Ink. The outcomes for variables were given in the form of rates (%). Chi Square was used for categorical variables that measured association among categorical variables. *P*-values less than 0.05 were considered significant.

Results: Malignant tumors accounted for 177/282 (62.8%) of the total kidney lesions, renal cell carcinoma (RCC) was the most common type of cancer with 126/282 (44.7%), followed by Wilms tumors 47/282 (16.7%), while non-Hodgkin's lymphoma reported 3 cases (1.1%) and mucinous carcinoma one case (0.35%). Benign tumors accounted for 14/282 (5%), and non-neoplastic lesions accounted for 91/282 (32.3%). Concerning RCC, the average diameter of RCC is 8.9 cm. GI 40/126 (31.7%) with mean tumor diameter equal to 5.8 cm; GII was the most frequent grade 63/126 (50%).

Conclusion: Renal cell carcinoma in Yemeni adults presents at an early age with an increased incidence among the female sex with a relatively larger tumor size. It appears that there has been a slight improvement in the diagnosis of kidney cancer in Yemen over the past 18 years.

Keywords: Benign tumors, grades, malignant renal tumors, non-neoplastic lesions, renal cell carcinoma (RCC) renal masses, Wilms' tumor (WT).

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INTRODUCTION

Around 208,500 new cases of kidney cancer are diagnosed in the world each year, accounting for just fewer than 2% of all cancers. The highest rates are recorded in North America and the lowest rates in Asia and Africa[1-3]. In Yemen, there are only some special epidemiological studies dedicated to malignancies[4-10], and for this motive it is necessary to strengthen, update, build and continue to bear the costs of studies on tumor

behavior with a plan to achieve a better impact on public health, with early diagnosis and appropriate treatment with a plan to enhance survival and reduce the possible subsequent consequences of malignancy. It was found that the preponderance of renal masses remain benign. However, a large number of them require further diagnosis and therapeutic interventions. At present, imaging methods such as magnetic resonance imaging, computed tomography, or ultrasound are used to diagnose these masses and classify them into solid or cystic[11-13].

Kidney masses have generally increased in the last two decades due to enhanced sensitivity and common use of advanced imaging methods. This is why this renal mass is more commonly diagnosed in healthy individuals today than it was 30 years ago. Alternatively, the ratio of recent malignant renal mass cases continued stable from 2008 to 2016, with the five-year survival rate progressively improving as a result of advances in detection and early intervention[1].

Kidney cancer begins in the kidneys with symptoms including blood in the urine, back pain and abdominal flatulence. Fever, weight loss, and fatigue are also common. A complication of these tumors is its spread to the lungs or the brain[1-3]. The most important types of kidney cancer are renal cell carcinoma (RCC), and Wilms carcinoma. RCC accounts for just about 80% of renal carcinomas[2]. Smoking, being overweight, high blood pressure, certain pain medications as non-steroidal anti-inflammatory drugs (NSAIDS), previous bladder cancer, certain chemicals, and family history are potential risk factors for RCC[2,3,13]. Genetic factors have little effect on an individual's susceptibility to infection with instant relatives of people with RCC having a 2 to 4 folds increased risk of develop RCC[14]. Further genetically related conditions rise the risk of renal cell carcinoma, consisting of hyperparathyroidism-jaw tumor syndrome, hereditary papillary renal carcinoma, Birt-Hogg-Dube syndrome, hereditary leiomyomatosis, von Hippel-Lindau disease, familial papillary thyroid carcinoma, and sickle cell disease[15].

Wilms' tumor, and identified as nephroblastoma, is a kidney cancer that usually occurs in children, and seldom in adults. Wilms' tumor has numerous causes, which can be generally classify as syndromic and non-syndromic. Syndromic causes of Wilms' tumor are caused by changes in genes such as the Wilms tumor 1 (WT1) or Wilms tumor 2 (WT2) genes, and the tumor appears with a range of other signs and symptoms. Non-syndromic Wilms' tumor is not connected with additional symptoms or pathologies. Numerous cases of Wilms' tumor develop from the nephrogenic rests. The nephrogenic rests are fragments of tissue in or around the kidney which they developed before birth and turn into cancerous masses after birth[16].

Yemen lacks a unified National Cancer Registration Center (NCRC) to date. Thus there is a need of cancer information and trustworthy data. For this goal, this study designed to illustrate the different types of kidney cancer, the gender and age distribution of the cancer, and to identify the different types of them and their association with gradation and invasion; and its association with age groups and gender, during the past eighteen years, based on data from two main pathology examination centers in Sana'a city, Yemen.

SUBJECTS AND METHODS

Study designed: Retrospective descriptive study.

Study site: The unit of cancer in Al-Thorah University hospital and the National Center for Public Health Laboratories (NCPHL) in the Departments of Pathology in Sana'a city which serve the major government hospitals and private hospitals in the city of Sana'a and act as reference laboratories for the entire country.

Study population: Study was conducted on renal lesion patients (patients are usually referred from hospitals for histological diagnosis) who were subsequently diagnosed selectively by histo-pathological study in the Department of Pathology at the National Center for Public Health Laboratories (NCPHL) and the unit of cancer in Al-Thorah University hospital Sana'a, Yemen, over a period of about 18 years from January 1, 2004 to December 31, 2021.

Operational variables: The cancer was classified according to the results of the tissue examination preserved in the paper records of each case before its entry into the SPSS program. The entry was reviewed by three different people to reduce the error during the entry of the collected data - and the sample size was determined by the number of patients diagnosed in the two selected units in the period between 2004 Until 2021, and the quality of the data was ensured by excluding any record of patients who lacked any of the variables on which the research was based on.

Study variables and cancer classification: The variables of the study were the histological type of cancer, sex, grades, and age. Types, grades, and histological diagnoses were formed in line with the World Health Organization[17] and "Kidney Cancer, Version 2.2017, NCCN Clinical Practice Guidelines in Oncology"[18].

Inclusion criteria: Inclusion criteria for patients included the following: complete renal histo-pathological findings, patients of any age and gender, availability of clinical data, and histological slides that confirm the diagnosis of kidney lesions and cancers.

Exclusion criteria: Patients with no histopathological slides and insufficient clinical data in the records were excluded.

Statistical analysis

Data were reported using suitable descriptive statistics (consisting of mean, frequency, standard deviation, *OR*, *CI*, X^2 and *P*-value). First data were entered using the SPSS software to minimize errors. All statistical analyzes of the data were performed using the Statistical Package for Social Sciences (SPSS) version 24 and Excel 2007.

Ethical approval

From the Faculty of Medicine and Health Sciences at Sana'a University, the Research and Ethics Committee with a reference number (811) dated 10-01-2022, the ethical approval was obtained. Also, all data, including patient identification, have been kept confidential.

Table 1: Gender and age distribution of kidney lesion patients in Sana'a, Yemen.

Characters	Number (%)
Gender	
Male	124 (44)
Female	158 (56)
Age groups	
Less than 1 year	2 (0.7)
1-15 years	58 (20.6)
16-30 years	51 (18.1)
31-45 years	68 (24.1)
≥46	103 (36.5)
Total	**282 (100)**
Mean age	36.4 years
SD	21.3 years
Min	9 months
Max	85 years
Mode	50 years
Median	40 years

RESULTS

The distribution of female cases increased by 56% than that of males (44%). The mean age of the study group was 36.4 years with SD equal to 21.3 years and ages ranged from 9 months to 85 years. Most of the lesions were in the age group ≥ 46 years (36.5%) followed by 31-45 years (24.1%), 1-15 years (20.6%) and 16-30 years (18.1%), while in less than 1 year there were only two cases (Table 1).

Table 2: Distribution of different renal lesions diagnosed between 2004-2021 in two oncology screening centers in Sana'a, Yemen.

Renal Lesions	Number (%)
Malignant tumors	**177 (62.8)**
Renal cell carcinoma	126 (44.7)
Wilms tumor	47 (16.7)
Non-Hodgkin's lymphoma	3 (1.1)
Mucinous carcinoma	1 (0.35)
Benign tumors	**14 (5)**
Angiomyolipoma	6 (2.1)
Ganglioneuroblastoma	1 (0.35)
Mesoblastic nephroma	2 (0.7)
Neurofibroma	1 (0.35)
Oncocytoma	4 (1.4)
Non-neoplastic lesions	**91 (32.3)**
Chronic pyelonephritis	77 (27.3)
Cystic renal disease	1 (0.35)
End stage kidney	5 (1.8)
Tubulo-intestinal-nephritis	2 (0.7)
Polycystic kidney disease	2 (0.7)
Simple benign cyst	3 (1.1)
Renal atrophy	1 (0.35)
Total	**282 (100)**

Malignant tumors accounted for 177/282 (62.8%) of the total kidney lesions, renal cell carcinoma (RCC) was the most common type of cancer with 126/282 (44.7%), followed by Wilms tumors 47/282 (16.7%), while non-Hodgkin's lymphoma reported 3 cases (1.1%) and mucinous carcinoma one case (0.35%). Benign tumors accounted for 14/282 (5%) which included angiomyolipoma (2.1%), ganglioneuro-blastoma (0.35%), mesoblastic nephroma (0.7%), neurofibroma (0.35%) and oncocytoma (1.4%). Non-neoplastic lesions accounted for 91/282 (32.3%), and they included chronic pyelonephritis (27.3%), cystic kidney disease (0.35%), end-stage renal failure (1.8%), tubulo-intestinal-nephritis (0.7%), Polycystic kidney disease (0.7%), simple benign cyst (1.1%), and renal atrophy (0.35%) (Table 2).

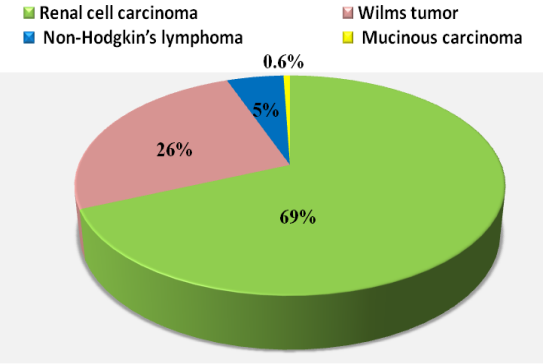


Figure 1: Distribution of different malignant tumors in two oncology screening centers in Sana'a, Yemen.

Malignant tumors accounted for 177/282 (62.8%) of the total kidney lesions, renal cell carcinoma (RCC) was the most common type of cancer with 126/177 (71.2%), followed by Wilms tumors 47/177 (26.6%), while non-Hodgkin's lymphoma reported 3 cases (5.3%) and mucinous carcinoma one case (0.6%) (Figure 1). Right kidney lesions were 140/282 (49.6%) and left kidney lesions were 142/282 (50.4%), and no cases of lesions on both sides (Figure 1, Figure 2). The average diameter of RCC is 8.9 cm. GI was 40/126 (31.7%) with mean tumor diameter equal to 5.8 cm, GII was the most frequent grade 63/126 (50%) with mean tumor diameter equal to 10 cm, GIII was 19/126 (15.1 %) and had a mean tumor diameter of 11 cm, while the GIV was only 4/126 (3.2%) with a mean tumor diameter of 12.4 cm (Table 3). Female cases were 71/126 (56.3%) more than male cases 55/126 (44%). The mean age of RCC patients was 49.9 years with SD equal to 13.5 years and ages ranged from 12 years to 85 years. Most of the renal cell carcinoma patients were in the age group ≥ 46 years (60.3%); followed by 31-45 years (34.1%), 16-30 years old had 6 cases (4.8%), while 1-15 years only had 1 case (0.8%) (Table 6).

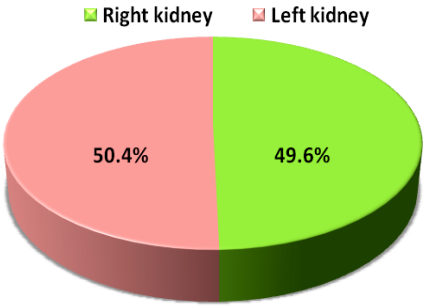


Figure 2: Side of the kidney with renal lesions in 282 patients in Sana'a, Yemen.

Table 3: Distribution of renal cell carcinoma according to the grade, among 126 renal cell carcinoma patients.

Staging	Number (%)	Mean Diameter of the Tumor (cm.)
GI	40 (31.7)	5.8
GII	63 (50)	10
GIII	19 (15.1)	11
GIV	4 (3.2)	12.4
Total	126 (100)	8.9

There was no significant association between RCC and gender as equal rates were found in both sexes. Considering the age groups, there was a highly significant association of RCC with the ≥46-year-old group as the rate was 73.8% with OR=7.2, CI=4.2–12.5, p<0.001. There was a highly significant association of RCC also with the 31-45-year group where the rate was 43% with OR =2.7, CI=1.5–4.7, p<0.001. There was no significant association between renal cell carcinomas with other age groups.

Table 4: Sex and age distribution of 126 RCC patients.

Characters	Number (%)
Gender M:F ratio = 1.0: 1.3	
Male	55 (43.7)
Female	71 (56.3)
Age groups	
1-15 years	1 (0.8)
16-30 years	6 (4.8)
31-45 years	43 (34.1)
≥46	76 (60.3)
Total	126 (100)
Mean age	49.9 years
SD	13.5 years
Min	12 years
Max	85 years
Mode	50 years
Median	50 years

Also, there was no significant correlation between renal cell carcinoma and the renal side, where approximately equal rates were found for both sides (Table 5).

Table 5: Association between RCC sex and ages among 282 patients with renal lesions.

Characters	RCC n=126 No (%)	*OR*	*CI 95%*	X^2	*p*
Gender					
Male n=124	55 (44.4)	0.92	0.57-1.4	0.11	0.73
Female n=158	71 (44.9)	1.02	0.77-1.3	0.009	0.92
Age groups					
Less than 1 year n=2	0 (0.0)	0.0	Undefined	1.6	0.2
1-15 years n=58	1 (1.7)	0.02	0.004-0.2	57	<0.001
16-30 years n=51	6 (11.8)	0.12	0.05-0.3	27.2	<0.001
31-45 years n=68	43(63.2)	2.7	1.5-4.7	12.4	<0.001
≥46 n=103	76 (73.8)	7.2	4.2-12.5	55.6	<0.001
Kidney side					
Right n=140	61 (43.6)	0.91	0.57-1.4	0.13	0.7
Left n=142	65 (45.8)	1.1	0.7-1.8	0.22	0.63
Total n=282	126 (43.8)				

OR = odd's ratio, *CI* 95% = confidence interval 95%, X^2 = Chi square, p= p value

DISCUSSION

Renal masses frequency

In the current study, the distribution of female cases increased by 56% than that of males (44%). This result is different from that reported elsewhere in which males are more infected with renal masses[11]. Also, most of the lesions in the current study were in the age group ≥46 years (36.5%) followed by 31-45 years (24.1%), 1-15 years (20.6%) and 16-30 years (18.1%), while in less than 1 year there were only two cases. These findings are similar to those reported elsewhere in the world where advanced age is a validating factor for benign tumors, malignancies, and/or non-neoplastic lesions[10,11,19,20]. Also, most regions of the world have seen increases in age-standardized incidence rates (rate of increase with age), with South Asia, tropical Latin America, and high-income Asia Pacific region reporting the largest increases. In contrast, the Caribbean and southern Latin America showed lower standard incidence rates for older adults[19]. In this study, malignancies accounted for 177/282 (62.8%) of the total kidney lesions (Table 2). This result differs from that reported in developed countries where benign masses are predominant[11,19]. The decline in the benign masses in current study is due to the small size of the benign masses that lead to be unrecognized and diagnosed. Active surveillance is suggested in various situations, in particular in tiny masses with benign characteristics. Once the tumor is less than 1 cm by a regular growth rate, more imaging and biopsy are not helpful because of the minimal risk of malignant transformation. These patients should be to have active surveillance as an alternative. Monitoring should also be offered to patients who are not candidates for surgery. A suitable candidate for active surveillance is elderly patient with a short life expectancy with a tumor size of less than 4 cm. Even though there are no standardized guidelines for the rate of active monitoring, the consensus is that renal ultrasound, CT scan, or MRI may be used to monitor renal mass every 3 to 6 months for the first year. They can be diverged depending on the kidney pathology and its progression[21-25].

Renal cell carcinoma (RCC)

In the current study, malignancies accounted for 177/282 (62.8%) of the total kidney lesions with renal cell carcinoma (RCC) being the most common carcinoma with 126/282 (44.7%) (Table 2). Renal cell carcinoma (RCC) is cancer of kidney that initiates in the lining of the proximal convoluted tubule, the part of the very small tubes in the kidneys that transport primary urine. RCC was the most common type of carcinoma with 126/177 (71.2%) (Figure 1) of the malignancies in the current study. This result is slightly lower than the prevalence of this type in other countries where RCC is the most common type of kidney cancer in adults, where it is responsible for about 90-95% of the cases[25]. The result of the study have demonstrated that the incidence of RCC among Yemeni females (71/126 (56.3%) VS male cases 55/126 (44%) with sex ratio M: F=1.0:1.3). This result is different from that reported by Luciani *et al.*,[26] where the male to female ratio was 1.5:1 but similar to that reported by Talek and Al-Faqih in Saudi Arabia on a group of 43 Saudi patients with renal cell carcinoma; where the ratio of M:F was 1.3:1[27]. However, the result of current study differs from that reported by Al-Falahi *et al.*,[10] previously in Yemen where they observed a 1:1 ratio[10]. This difference between ratio of female and male is probably related to the different incidence of RCC risk factors in Yemeni both males and females. The known risk factors for the most predominant form of KC, renal cell cancer, include hypertension, smoking, obesity, as well as some other less important factors like familial history of KC, environmental and occupational exposure to genotoxic agents or nephrotoxic agents agents acrylamide, cadmium and trichloroethylene, low physical activity, chronic pharmacotherapy with diuretics and phenacetin, alcohol consumption[19,23,25] . Although these factors affect the incidence trend of KC, the relative impact of each factor may vary in different populations.

The mean age of RCC patients was 49.9±13.5 years and ages ranged from 12 years to 85 years and most of the renal cell carcinoma patients were in the 3rd and 5th decades and there was a highly significant association of RCC with the ≥46-year-old group as the rate was 73.8% with OR=7.2, CI=4.2–12.5, p<0.001 and with the 31-45 year group where the rate was 43% with OR=2.7, CI=1.5–4.7, p<0.001 (Table 4). Thus, the peak incidence of RCC occurs about two to three decades lower than the peak incidence of 50-70 years reported among Caucasians[28], but is almost similar to that previously reported in Yemen where the mean age was 50.3±13.3 (range 22-80), with a peak incidence in the fourth and fifth decades of life[7]. About 40% of total patients are under 40 years of age, and this finding is about eight times greater than that reported by Jae Hee Suh *et al.*, in a cohort of 838 RCC cases[29], only 5.2% of their patients had ≤40[29]. This indicates a higher incidence of renal cell carcinoma in younger adults (40 years old) in Yemen. Renal cell carcinoma causes about 15,000 deaths or 80% of all kidney and pelvic cancers. As with most other types of cancer, survival improves with early diagnosis and treatment. According to the American Cancer Society, the survival rate for localized disease in grades 1 and 2 is over 90%, while the survival rate for distant metastasis, as in stage 4, is 13% for 5 years. In the third stage, the survival rate for patients who underwent nephrectomy reaches 70%. However, invasion into the renal vein indicates a poor prognosis[30,31].

Presentation by grade is compared with other series in (Table 3) 81.7% of used patients presented in GI and GII and 18.3% in GIII and GIV. These results are consistent with other reports and indicate that there is no delay in the diagnosis and management of renal cell carcinoma patients in Yemen. The average size of the surgically removed tumor mass in this series was 8.9 cm (ranged 3–18 cm); for the GI was 5.8 cm, the GII was 10 cm, the GIII was 11 cm, and the GIV was 12.4 cm (Table 3). The tumor size ranged from 5 to 8 cm in most of the series, and the average size reported in the literature was 5.3 cm[10, 11,19,20]. This finding in Yemeni patients indicates that in used community RCC is relatively larger at presentation. This finding also reflects late presentation in most of used patients in contrast to early detection in developed societies[11,19,21].

CONCLUSION

Renal cell carcinoma in Yemeni adults appears at an early age in the fourth and fifth decade with an increased incidence among females with a relatively larger tumor size compared to other regions of the world. Current study provided much needed information about the burden of kidney cancer in Yemen, to enable Yemen to better plan to address the burden. Further studies are necessary to determine the exact incidence, trend of KC, and risk factors in Yemen.

AUTHOR'S CONTRIBUTION

This study was completed by Amin Abdulkarem Okbah, Professor of Histopathology at Sana'a University, and the National Center of Public Health Laboratories (NCPHL) Sana'a, Yemen; and Prof. Dr. Hassan Abdul-Wahab Al-Shamahy, Faculty of Medicine, Sana'a University. All authors analyzed the data, wrote the manuscript, and reviewed it.

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CONFLICT OF INTEREST

No conflict of interest associated with this work.

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