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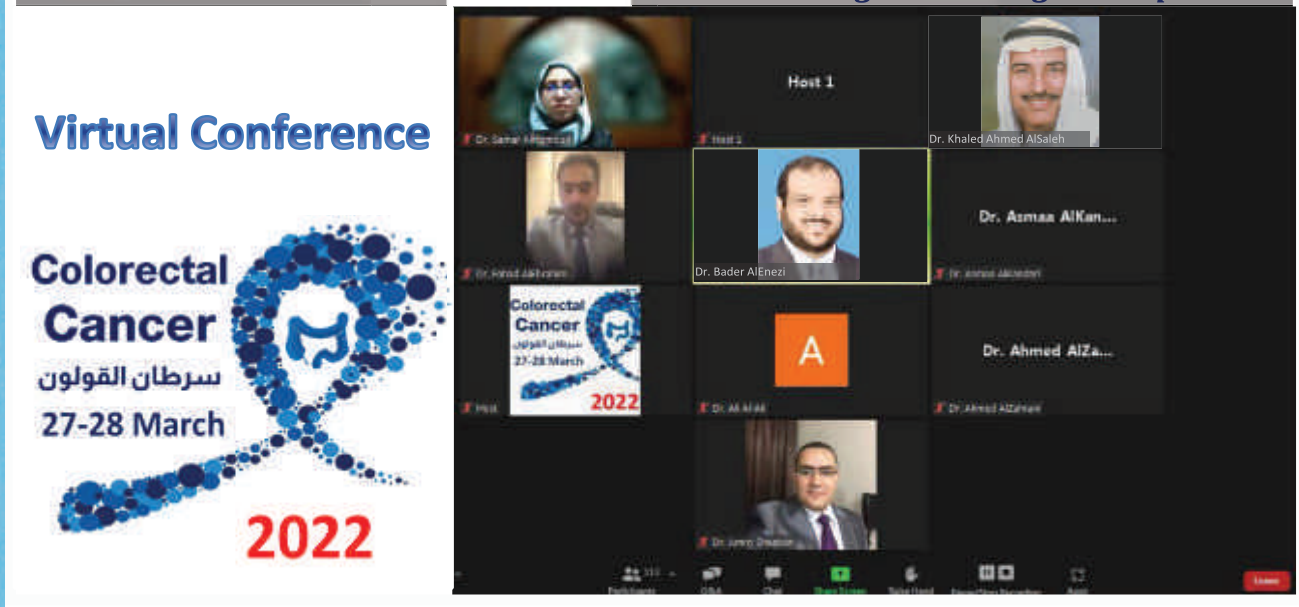

The Official Journal of the Gulf Federation For Cancer Control

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Original Article

Epidemiology of Cancer Among Chronic Kidney Disease Patients Compared to The General Population

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Abstract

Background: Kidney disease has a major effect on global health, both as direct cause of morbidity and mortality and as an important factor for other comorbid diseases including malignancy. Different studies report a higher risk of cancer development in patients with chronic kidney disease (CKD), but the impact of less sever CKD on risk of cancer is uncertain. However, data concerning the cancer risk in Oman CKD including dialysis patients is scarce. More importantly, there is lack of information about the cancer–specific mortality in CKD and dialysis patients.

Methods: During January 2006 to December 2019, all patients with CKD and those on regular dialysis who are admitted or follow up in Royal Hospital were included for evaluation of malignancy.

Results: During the study, a total of 2500 patients with CKD were included, of which 25 patients were found to have different types of cancers, of which 13 were male (52%) and 12 were female (48%).Most of patients 13 (52%) were senior adult (>65 years), then 11 (44%) were adult (19:64–ys) and only one case (4%) was child (<18years.). Cancer was detected in the ovaries (16%), stomach, multiple myeloma and renal (12%) each, while breast and colorectal (1 male/1 female) (8%), parathyroid, thyroid, uterus, cervix, prostate, skin, liver, lymphoma, pituitary gland, and myelofibrosis were present in 4% each. In general population, the breast cancer is the most common cancer among females, followed by thyroid cancer, and colorectal cancer while the most common cancer types among males are colorectal cancer followed by the prostate and then the Non–Hodgkin lymphoma disease.

Conclusion: These epidemiologic findings should prompt clinicians and health authorities to assess strategies for cancer screening in high–risk population of CKD patients. Additional studies are needed to explain the reasons for this association and represent the potential use of cancer screening in patients with CKD in Oman.

Key words: cancer, chronic kidney disease, epidemiology, hemodialysis

Introduction

Oman is the second largest country in the South East of Arabian Peninsula (309,500 square kilometers) with a relatively small and young population (4,425,000 people). In Oman, there has been a progressive increase in the end–stage kidney disease (ESKD) incidence and prevalence over the last few decades. The World Health Organization (WHO) ranked Oman on the 51st position of the top world countries where CKD is the most important causes of death and reported that CKD was the 6th major cause of death of total deaths accounting for 2.97% of total deaths (18.1 per 100,000 populations) (World Health Organization. Health Profile: Oman– Accepted 9 April 2016).(1) Through the last 4 decades, there was a sharp progression in the prevalence of people progressing to ESKD and demanding renal replacement therapy (RRT) has been noticed in Oman (2, 3). The incidence rate of ESKD patients receiving RRT in Oman was 21, 75, 120, and 160 per million population (PMP) in 1983, 2001, 2013 and 2019, respectively. Similarly, the prevalence of ESKD was 49, 916, 2386, and 4117 in 1983, 2001, 2013 and 2019, respectively. Along with the increasing rate of ESKD, a gradual increase in morbidity caused by CKD had been observed (2/3).

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The Gulf Cooperation Council (GCC) member countries include Bahrain, Kuwait, Oman, Qatar, Saudi Arabia, and United Arab Emirates. The GCC population is estimated to be about 56 million, ranging from 1.5 million in Bahrain to 33.4 million in Saudi Arabia. Oman has the second highest incidence of cancer in the GCC in general population. Of the 71,882 newly– diagnosed cancer cases reported by the GCC National Cancer Registries, Oman accounted for 7,938 cases (11%), Saudi Arabia held the top spot with a 71.8 % (51,587 cases) of the total cases, Kuwait was placed third with 7.1%, followed by Bahrain (4.6%), the UAE (3.5%) and Qatar (1.9%) [4].

Between January 1996 and December 2015, there were 21,002 newly diagnosed cases of cancer among the Omani population with an average of 1050 cases per year [4]. The frequency and incidence rates of cancers in Omani male and female are presented in **table 1.**

Gender	Frequency	Percentage (%)	Average annual crude rate	Average annual ASR
Male	10.723	51.1	55.1	105.2
Female	10.279	48.9	54.2	96.3
Total	21.002	100	56.4	125.7

Table 1: Shows the frequency and incidence rates of cancer in Omani population.

Over a 20–year period (1996–2015), breast cancer was the leading cancer followed by Non–Hodgkin lymphoma, Leukemia, colorectal and thyroid, as shown in table 2.

Topography	Frequency	Percentage (%)
Breast	2,280	10.9
Non–Hodgkin lymphoma	1,533	7.3
Leukemia	1,439	6.9
Colorectal	1,382	6.6
Thyroid	1,277	6.1

Table 2: Shows the frequency and percentage of different cancer among Omani population.

Information concerning the cancer mortality among CKD patients and in dialysis patients is lacking. Here, we are conducting a study to examine the development of various types of cancers among the Omani chronic kidney disease patients who had not undergone transplantation compared to Omani general population.

Materials and Methods

The Royal Hospital in Oman has an excellent medical record and information technology system where everything is computerized and had received a well–recognized international certificate of excellence for its achievement in its IT system called Al Shifaa. All clinical and various laboratory data are collected progressively. During January 2006 to December 2019, all patients with CKD and ESKD on regular dialysis who are admitted or follow up in Royal Hospital were included for evaluation of malignancy. The study was approved by the Medical Ethics and Research Committee at the hospital with an approval number of SRC#6/2019.

Information collected for analysis include age in years (1=Children 00–18, 2= adult 19–64, 3=Senior 65 &over), sex, nationality (Omani/Non–Omani), body weight (kg), height (cm), and body mass index (BMI) (weight in kg divided by height in meter squared kg/m^2). The WHO classification for BMI was used to estimate the degree of obesity, duration of signs and symptoms (months), presence or absence of edema at time of presentation, clinical evidence of urine changes (change in color, amount, form and frequencies), blood pressure (BP) (mm Hg), Diabetes mellitus (type 1 or 2) and duration (years) of diabetes, presence of uremic signs and symptoms at time of presentation and if renal replacement therapy in the form of hemodialysis was needed or not.

Clinical examination, by multidisciplinary team, was carried on for all patients. Laboratory investigations included the following: serum creatinine (SCr), blood urea nitrogen (BUN), estimated glomerular filtration rate (eGFR), serum sodium, serum potassium, serum chloride, bicarbonate level, bone profile, serum magnesium, serum albumin, total serum protein, hemoglobin level, total white cell count (WBCs), fasting serum glucose level, glycated hemoglobin (HbA1c), and lipid profile. Urine investigations included urinary protein/creatinine ratio (UPCR) (mg/mmol, normal <20, overt proteinuria 20–200, nephrotic >200), total protein in the urine (mg/dL), and total blood in the urine (ERY/µL). In addition, radiological data regarding kidney ultrasound and chest X–ray at admission time were included. Kidney ultrasound examination was done at the diagnostic radiology department to identify the kidney size, detect and grade kidney parenchymal echogenicity and to exclude the presence of associated kidney disorders such as stones, masses, and hydronephrosis. It was done by expert sonographers with the patient in supine position. Axial and sagittal images were taken. The length of each kidney was measured in the sagittal plan. The kidney parenchymal echogenicity was estimated compared to the hepatic and splenic echogenicity. Chest X–ray was examined for possible chest infection, pleural effusion, cardiomegaly, and metastasis.

Renogram and echocardiology findings were examined during the same admission time. CT chest for possible

abnormal findings; metastatic mass, lymph nodes, pleural effusion and pericardial effusion were also studied same as for CT abdomen and pelvis.

We studied the cancer in detail regarding age at cancer was diagnosed, methods of diagnosis; biopsy/ image, management strategies; conservative, chemotherapy, surgical intervention, radiotherapy, or combined treatment.

Two clinicians entered the data and rechecked by other two team members. Statistical analysis done using STATA software, Chicago, USA. Data described as frequencies and percentages of categorical variables. Continuous variables reported as median and ranges or as mean and standard deviation.

Results

During the study, a total of 2500 patients with CKD were included, of which 25 patients were found to have different types of cancers, of which 13 were male (52%). and 12 were female (48%)

Most of patients 13 (52%) were senior adult (>65 years), then 11 (44%) were adult (19:64–ys) and only one case (4%) was child (<18years), as shown in figure 1.

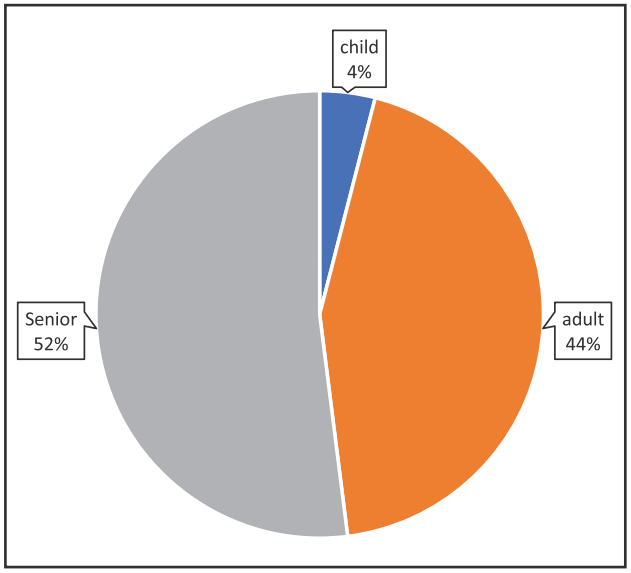


Figure 1: Shows the Patients age during the study period.

The mean (SD) weight was 66 (±26) kg, minimum was 38 kg and maximum were 94 kg. Most studied patients were above average weight; 6 patients were overweight (24%), 4 patients with class I obesity (16%) and 4 patients were class II obesity (16%), while 8 patients were with average weight (32%) and only 3 patients were under weight (12%).

The number of patients presented with acute symptoms (<3months) were 13 patients (52%) and 12 patients (48%) presented with chronic symptoms (>3months). Most common symptoms at presentations were: dyspnea in 8 (32%) patients, GIT signs and symptoms in 5 (20%) patients, generalized body ache in 5 (20%) and uremic signs and symptoms in 2 (8%) patients, 5 (20%) patients presented with other manifestations like fever, hematuria, lower limb edema, vaginal urine leak and gynecomastia.

Hypertension was the major comorbidity in 21 (84%), and diabetes mellitus in 12 patients (48%). Most studied patients were with advanced kidney impairment at time of presentation, 10 patients (40%) in CKD stage III, 9 (36%) patients in CKD stage V and 3 (12%) patients in CKD stage IV while there were 2 (8%) patients in CKD stage II and only one patient (4%) in CKD stage I. A total of 8 (32%) patients were in need for renal replacement therapy in the form of conventional hemodialysis. Furthermore, majority (64%) of patients had high PTH level, 60% had low serum albumin, 76% had anemia, and 48% had high HBA1C level.

Chest X–ray revealed no lung infection in 100% of patients, while pleural effusions were present in 40% and cardiomegaly in 52%.

Ultrasonography examination showed that 16% had a kidney size >11 cm, 44% of patients had a kidney size between 10 and 11 cm in length, 8% of patients had kidney size between 9 and <10cm, and 32% had a kidney size of 8 cm and less. Kidney echogenicity was increased in 13 patients (52%). Kidney cysts were present in 8 patients (32%). Loss of corticomedullary differentiation was detected in 17 patients (68%). Kidney stones were present in only two patients (8%).

Renogram showed evidence of obstruction in only one patient.

Echocardiography among studied patients revealed low ejection fraction (EF) <55% in 6 (24%) patients, left ventricular hypertrophy in 14 (56%) patients, diastolic dysfunction in 12 (48%) patients, mitral valve regurgitation (MVR) in 14 (56%) patients, aortic valve regurgitation (AVR) in 6 (24%) patients, tricuspid valve regurgitation (TVR) in 13 (52%) patients, pulmonary valve regurgitation (PVR) in only one (4%) patient and pericardial effusion in 3 (12%) patients.

The chest computerized tomography (CT) showed abnormal findings in 70% of scanned patients. Pleural effusion was present in 3 (12%) patients, abnormal masses, enlarged lymph nodes, pericardial effusion, and pulmonary fibrosis were present in 16% each.

The CT abdomen and pelvis revealed abnormal findings in 14 (56%) patients, 9 (36%) patients with enlarged abdominal masses, 2 (8%) patients had ascites, whereas enlarged lymph nodes and bilateral distal ureteric injury

Test	ALL mean	Standard deviation	Minimum	Maximum
Serum creatinine	318.8 umol/L	258.6	67 umol/L	863 umol/L
Blood urea	13.9 mmol/L	10.1	3.4 mmol/L	35 mmol/L
GFR	33.2 mL/min/1.73 m2	26.1	4 mL/min/1.73 m2	90 mL/min/1.73 m2
Serum potassium	4.2 mmol/L	0.6	2.4 mmol/L	5.5 mmol/L
Serum sodium	135.4 mmol/L	5.2	117 mmol/L	142 mmol/L
Serum carbon dioxide	20.8 mmol/L	5.1	8 mmol/L	28 mmol/L
Serum corrected Calcium	2.3 mmol/L	0.3	1.7mmol/L	2.8 mmol/L
Serum phosphate	1.4 mmol/L	0.6	0.7 mmol/L	2.9 mmol/L
Alkaline phosphatase	134.5 iU/L	101.3	50 iU/L	512 iU/L
Parathyroid hormone	33 pmol/L	33.9	2.1 pmol/L	82.6 pmol/L
Serum magnesium	0.72 mmol/L	0.14	0.61 mmol/L	0.87 mmol/L
Serum albumin	31.7 g/L	6.1	19 g/L	41 g/L
Total protein	67.3 g/L	11.1	52 g/L	104 g/L
Hb level	10.3 g/L	2.2	7.3 g/L	16 g/L
Platelet count	264.3 10*9/L	95.9	110 10*9/L	400 10*9/L
WBCs	7.9 10*9/L	5.3	2.8 10*9/L	10*9/L 22.9
Plasma glucose	7.3 mmol/L	3.9	3.9 mmol/L	16.8 mmol/L
HBA1C panel	9.6 %	5.1	4.3%	14.5%
Triglyceride level	1.25 mmol/L	0.5	0.8 mmol/L	1.7 mmol/L
Total cholesterol level	4.3 mmol/L	1.5	3 mmol/L	6.3 mmol/L
LDL level	2.6 mmol/L	0.9	1.7 mmol/L	3.9 mmol/L
HDL level	1.17 mmol/L	0.7	0.51 mmol/L	2 mmol/L
UPCR level	93.8 mg/mmol	125.3	0 mg/mmol	333 mg/mmol

Table 3: Shows the mean (stand deviations, minimum and maximum of different laboratory findings at time of diagnosis)

HBA1c: Glycated hemoglobin, CI: Confidence interval, eGFR: Estimated glomerular filtration rate, HB: Hemoglobin, WBCs; White blood cells, LDL: Low–density lipoprotein, HDL: High–density lipoprotein, UPCR: Urine protein–to–creatinine ratio

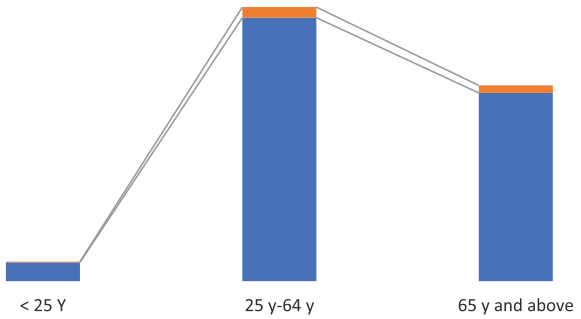
with urinoma was present in (8%) each. Cancers were detected in the ovaries (16%), stomach, multiple myeloma and renal (12%) each, while breast and colorectal (8%), parathyroid, thyroid, uterus, cervix, prostate, skin, liver, lymph nodes, pituitary gland and myelofibrosis were present in 4% each.

Biopsy (Histopathology) was the most reliable methods used for cancer diagnosis in our study, 19 (76%) patients, while imaging used only in 6 (24%) patients.

The main two types of cancer treatment used in this study were Chemotherapy &Hormonal therapy in 10 (40%) patients and Surgery in 9 (36%) patients. while 5 (20%) patients kept with conservative management and lastly radiation was done in only one (4%) patient.

Figure– 2–shows age distribution at time of diagnosis. A total of 14 (56%) patients were in the age between 25 and 64 Years old, 10 (40%) patients were 65 and above

Figure 2. Shows the age of participants at time of diagnosis



and only 1 (4%) patient was at age of < 25 years old at time of diagnosis. Mean age of diagnosis is 56.3 year (min. 15 y and max. 89 y) with standard deviation of 16.1 years.

A total of 10 (40%) patients passed away within 5 years after diagnosis, while 7 (28%) patients passed away after 5–10 years and 8 (32%) patients after > 10 years with mean age at death was 68 year (min. 54–year, max. 90 year).

Discussion

This is the first study that evaluates the epidemiology of cancer among chronic kidney disease patients compared to general population in Sultanate of Oman over a decade period. These patients underwent through clinical, laboratory and imaging evaluation. CKD and cancer are both major and growing public health problems nationally and internationally. A long time ago, the links between renal disease and malignancy were observed, however, quite recently their importance was recognized and 'new' subspecialty in nephrology, namely 'Onconephrology' was established [5]. In this present study, cancer such as ovary (16%), stomach, multiple myeloma and renal (12%) are the most common sites of cancer in CKD population. Table– 4

Common cancers in Oman	Male	Female
General population	1– Colorectal 2– Prostate 3– Non–Hodgkin Lymphoma (NHL)	1– Breast 2– Thyroid 3– Colorectal
CKD patients	1– Renal (Renal cell carcinoma (RCC) and bladder) 2– Multiple Myeloma 3– Prostate	1– Ovary 2– Stomach 3– Breast

Table 4: shows different types of cancer in Oman regards gender, general population, and CKD.

The Ministry of Health (MOH) represented by the National Cancer Registry (NCR) recently issued its annual Cancer Incidence Report in Oman for 2017. The report indicated that the number of recorded tumors cases in 2017 reached 2101 including 1892 (90.05%) cases among Omanis, 188 (8.95%) cases among residents, and 19 (0.9%) cases of Carcinoma in situ among Omanis. the breast cancer is the most common cancer among females in the Sultanate, followed by thyroid cancer, and colorectal cancer while the most common cancer types among males are first colorectal cancer followed by the prostate and then the Non–Hodgkin lymphoma disease [6]

Al–Lawati and colleagues [5] reported that from 1996 to 2015, over 21000 cases of cancer were registered among Omanis, with an average of 1050 cases/year. The frequency of cases among both genders was similar (51% men vs. 49% women).

One of the most important complications and cause of morbidity and mortality in CKD patients is cancer. Prevalence of cancer in CKD increases with age. In the present study, the mean age at time of cancer diagnosis was 56.28 year, of which 14 Patients (56%) in the age between 25–64 year, 10 patients (40%) were 65 –year old and above while only one patient (4%) was diagnosed at age of < 25 year. The type–specific incidences were also higher than the general population, and this might be related to the increased age of the CKD group. Therefore, clinicians should consider appropriate cancer screenings based on age in pre–dialysis CKD patients. In other study in USA, Iff et al. [7] also reported that, in older people, eGFR <60 mL/min/1.73 m2 is associated with an increased risk of cancer death with a linear relationship between reduction in eGFR and incidence of cancer–specific mortality. In contrast, In the international collaborative study, the excessive cancer risk was found to be the highest in the younger dialysis patients, gradually declined with increasing age and became only slightly elevated in the dialysis patients within the oldest age group in all registry population [8].

Nowadays, gender–specific issues and how they affect health have increasingly attracted public attention and those working with healthcare and prevention. In our study there was an overall male predominance (52%), as reported by Wong et al. [9] both male and female are equally affected by cancer (with a little high incidence in male) as in general population. As in a cohort of approximately 3600 participants, male–rather than female– had a significantly increased risk of cancer with lower GFR [9]. Furthermore, the gender effect on the relationship between dialysis modality and the renal outcome of patients with cancer remains unexamined.

In our study, 56% had obesity. A cohort Korean study by Nam et al [10], demonstrated positive association of BMI and waist circumference (WC) with CKD and Cancer development. Consistently, positive association between obesity and CKD with cancers have largely come from studies in the western population (10/11/12). 52% of patients presented with short duration of signs and symptoms, less than three–month duration. The most common clinical presentation was shortness of breath and dyspnea (32%), 20% had GIT signs and symptoms, 20% with generalized body ache, 4% with fever, same as for erectile dysfunction, vaginal urine leak, lower limb edema, and hematuria.

Most studied patients were having hypertension (84%) at time of diagnosis of cancer. Because hypertension may cause or result from CKD, HTN prevalence is higher and its control become more difficult with worsening of kidney function. Also, a retrospective cohort study [13], revealed

that new onset hypertension, regardless of severity, was observed in about one–third of cancer patients with various types of solid tumors and chemotherapy usage, appeared to be associated with an elevated risk of hypertension at each severity level. In the present study, hypertension was already established in most of patients at time of cancer diagnosis and this carries another overburden for these categories of patients with CKD and cancer in comparison with general population with cancer without CKD.

Diabetic nephropathy is a leading cause of end–stage kidney disease nowadays. Certain cancers are more common in patients with diabetes mellitus, many studies showed that certain types of cancer are more common in patients with type 1 or type 2 DM [11, 12]. In addition, T2DM has also been shown to be associated with cancer mortality [14]. However, there are not enough data concerning the cancer pattern in patients with diabetic nephropathy (DN). A study of 5643 DN patients was conducted in Hong Kong between 2000 and 2015 revealed that overall cancer incidence was similar between DN patients and the general population [15]. However, certain site–specific cancers are increased in DN patients such as cancers of larynx, liver, and colorectum in our cohort. Positive association of laryngeal cancer with either DM or CKD was rarely reported in literature.The threshold of kidney dysfunction at which the risk of cancer begins is approximately an eGFR of 55 ml/ min, and risk increases linearly as the eGFR falls, reaching a maximum three–fold increased risk with GFR 40 ml/min per 1.73 m2, which is similar to the risk increase seen in dialysis patients [16]. Similarly, in this study, where prevalence of cancer is higher in CKD stage IIIa and in dialysis patients, with mean e GFR of 33 ml/min/m^2; stage III CKD was an independent risk factor for cancer, and this risk increased in a linear fashion with lower baseline eGFR [9].

A study, using US adult patients enrolled in Medicare's ESKD program hemodialyzed within the period from April 1, 1995, through December 31, 2009, assessed the 5–year cumulative cancer incidence since start of RRT [17]. They reported that the 5–year cumulative incidence of any malignancy was 9.48% and was elevated for certain subgroups: elderly, non–Caucasians, non–Latino, males, nondiabetics, and recent hemodialysis therapy. They also suggested a high burden of malignancy in the hemodialyzed population compared to the US general population.

Lin et al. used the data from the Taiwan National Health Insurance Research Database on subjects who initially received RRT between January 1997 and December 2004, they showed that the RRT group revealed a significantly higher incidence rate than did the general population and risk for blood, liver, colorectal, oral, breast, renal, upper urinary tract, and bladder cancer development was significantly higher than in the general population [18].

In Europe, Bechade et al. used the data from cancer registries and hospital databases in one French region and searched for subjects with an incident malignancy between 2001 and 2008 who started RRT [31]. They found that the incidence rate of RRT in the population of incident malignancy was 370 per million population/year [19].

There are several explanations for increased cancer incidence in the dialysis population such as ESKD–associated immunodeficiency and nutritional abnormalities [16, 18]. Interactions between immune dysfunctions due to uremia and ESKD with established risk factors such as UV radiation, tobacco, or alcohol may also contribute to the excess cancer risk in CKD [20]. Recently, there has been a focus on the potential role of erythropoietin–stimulating agents, commonly used to manage anemia in CKD; known to activate erythropoietin receptors on the surface of cancer cells. Additionally, erythropoietin–induced angiogenesis may promote tumor growth [21].

Nephrologists who care for ESKD population face various challenges including delays in diagnosis of malignancy, unclear utility of malignancy screening, and dilemmas in diagnostic imaging [22] . In addition, in a case of advanced or refractory malignancy, both nephrology and oncology specialists may cope with the issue of ethically complex palliative care as well as withholding of RRT [23]. There are several confounding factors which may affect the diagnosis and evaluation of cancer in ESKD such as delayed symptomatic presentation, and utilization of un–validated and unclear utility of tumor markers, dilemmas in imaging studies, and lack of availability of prognostic data [24].Cengiz etal reported that in the last 20 years, prevalence of solid tumors was 6.7% in the population of 2817 subjects with CKD, including 199 subjects on hemodialysis [25]. It is of interest that 71% of the hemodialyzed patients were diagnosed with tumors in the first year of the RRT, while in 84% of patients with CKD, tumors were detected in less than 10 years after diagnosis of CKD. The most common were urologic malignancy followed by parathyroid adenoma and skin cancer in this studied population [25].

Most cancer surveillance and treatment trials exclude the CKD population, and it is unclear whether changes in standard screening practices and early diagnosis would reduce mortality in these patients. Therefore, in the absence of specific guidelines, patients with CKD should be screened for malignancies according to guidelines applicable to the general population. However, in the ESKD population, the benefits and cost–effectiveness of age–appropriate cancer screening are limited since

these patients have reduced life expectancy due in part to dialysis–associated comorbid illness. It appears to be preferable to tailor screening protocols based on the individual patient's risk factors and expected survival on dialysis [22].

Kidney disease has an impact on many of the imaging techniques and laboratory examinations used for the screening, diagnosis, or staging of cancer. For instance, the increase in vascular calcifications common in CKD may limit the interpretability of mammograms in women with ESKD[26]. Furthermore, certain tumor markers are cleared or metabolized by the kidney and become unreliable in the setting of kidney disease. As a result, carcinoembryonic antigen levels are falsely elevated in ESKD patients. The usefulness of cancer–associated carbohydrate antigens (CA 19–9, CA 50, CA 125, CA 15.3) as biomarkers has also been questioned. CA 125 may increase in the setting of peritonitis in patients using peritoneal dialysis modalities. Increased levels of serum alpha–fetoprotein and total prostate–specific antigen (PSA) remain highly specific in ESRD patients. As free PSA accumulates due to the decreased glomerular filtration rate (GFR) inherent in kidney disease, it becomes a less reliable marker [27].

The most reliable methods used for diagnosis of cancer in this study was Biopsy (Histopathology), (76%) were diagnosed after tissue biopsy, same as in general population. Nearly 20% of our patients presented with advanced cancers (12% of males and 11% of females presented with distant metastasis, and 7% of males and 9% of females presented with regional metastasis), compared to 26% of our CKD in this study at clinical presentation.

Treating cancer patients who are undergoing hemodialysis, or who have CKD, is a multidisciplinary effort. Oncologists and nephrologists need to coordinate with each other and with various healthcare team members to manage the complexities of the patient's medical problems. Cancer treatment can include localized therapies, such as surgery, radiation therapy, cryotherapy, and heat or chemical ablation, and/or systemic therapies (e.g., chemotherapy, hormonal therapy, immune therapy, and targeted therapy) used alone or in combination [28].

The main two types of cancer treatment used in this study were Chemotherapy &Hormonal therapy 10 (40%) patients and Surgery 9 (36%) patients as in general population. while 5 (20%) patients kept with conservative management and lastly radiation only one (4%) patient. Side effects that arise during treatment improve afterward for many patients but persist for others. The most common side effects of cancer and its treatment are pain, fatigue, and emotional distress [29].

In our study mortality rate was equal in both male and female. Five–year mortality rate was high (40%) compared to Omani general population (death certificate in 0.7% from all cancer cases) with increase among ESKD patients rather than other CKD stages. While 32% had > 10–year survival and 28% had 5–10–year survival.

The major strength of this study was the ability to assess cancer epidemiology and risk in one of the largest cohorts of individuals with CKD and on dialysis in comparison to general population in Oman.

The limitations of this study are: Any of the serum creatinine based GFR estimating equations may provide imperfect measurements of GFR (as MDRD which used in our study), introducing the potential for misclassification of kidney function level. We sought to minimize this misclassification by using longitudinal, time–updated measurements of GFR calculated by the CKD–EPI equation and isotope dilution mass spectrometry[30].

Data were also unavailable for selected over–the–counter analgesics, Chemotherapy, and hormonal therapy side effects in our studied patients.

Finally, our study sample was small number, so results may not be fully generalizable to other populations and practice settings.

Conclusion

A wide variety of cancer can occur at many sites in patients with CKD before and after RRT. Patients on dialysis and individuals with CKD also experience an excess risk for a number of tumors. Currently, there are no evidence–based cancer screening recommendations tailored for patients with CKD worldwide. These epidemiologic findings should prompt clinicians and health authorities to assess strategies for cancer screening in high–risk population of CKD patients. Additional studies are needed to explain the reasons for this association and represent the potential use of cancer screening in patients with CKD.

The management of cancer patients who are undergoing hemodialysis, or who have CKD, is multidisciplinary effort. Oncologists and nephrologists need to coordinate with each other and with various healthcare team members to manage the complexities of the patient's medical problems.

Compliance with Ethical Standards

Disclosure of potential conflicts of interest: The study was approved by the Scientific Research Committee at the Royal Hospital, Muscat, Oman and certify that the study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments ethical standards. https://mohcsr.gov.om/my–researches/

Informed consent: Each participant was freely given, informed consent to undergo biopsy and laboratory investigations.

Availability of data and material: Data of this paper is not available publicly but can be requested from the corresponding author in a reasonable time.

Funding: No funding available for both authors.

Conflict of Interest: Authors declare no conflict of interest.

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References

1. World Health Organization. Health Profile: Oman– Accepted 9 April 2016
2. Al Alawi I, Al Salmi I, Al Mawali A, Al Maimani Y, Sayer JA. End–Stage Kidney Failure in Oman: An Analysis of Registry Data with an Emphasis on Congenital and Inherited Renal Diseases. Int J Nephrol. 2017;2017:6403985.
3. Al Alawi IH, Al Salmi I, Al Mawali A, Sayer JA. Kidney Disease in Oman: a View of the Current and Future Landscapes. Iran J Kidney Dis. 2017;11(4):263–70.
4. Al–Lawati JA, Al–Zakwani I, Fadhil I, Al–Bahrani BJ. Cancer Incidence in Oman (1996–2015). Oman Med J. 2019;34(4):271–3.
5. Salahudeen AK, Bonventre JV. Onconephrology: the latest frontier in the war against kidney disease. J Am Soc Nephrol. 2013;24(1):26–30.
6. Department of non–communicable disease,Ministry of Health ,Oman.cancer incidence in Oman 2017.Ministry of Health 2020.
7. Iff S, Craig JC, Turner R, Chapman JR, Wang JJ, Mitchell P, et al. Reduced estimated GFR and cancer mortality. Am J Kidney Dis. 2014;63(1):23–30.
8. Maisonneuve P, Agodoa L, Gellert R, Stewart JH, Buccianti G, Lowenfels AB, et al. Cancer in patients on dialysis for end–stage renal disease: an international collaborative study. Lancet (London, England). 1999;354(9173):93–9.
9. Wong G, Hayen A, Chapman JR, Webster AC, Wang JJ, Mitchell P, et al. Association of CKD and cancer risk in older people. J Am Soc Nephrol. 2009;20(6):1341–50.
10. Nam GE, Cho KH, Han K, Kim CM, Han B, Cho SJ, et al. Obesity, abdominal obesity and subsequent risk of kidney cancer: a cohort study of 23.3 million East Asians. British journal of cancer. 2019;121(3):271–7.
11. LeRoith D, Novosyadlyy R, Gallagher EJ, Lann D, Vijayakumar A, Yakar S. Obesity and type 2 diabetes are associated with an increased risk of developing cancer and a worse prognosis; epidemiological and mechanistic evidence. Experimental and clinical endocrinology & diabetes : official journal, German Society of Endocrinology [and] German Diabetes Association. 2008;116 Suppl 1:S4–6.
12. Vigneri P, Frasca F, Sciacca L, Pandini G, Vigneri R. Diabetes and cancer. Endocrine–related cancer. 2009;16(4):1103–23.
13. Fraeman KH, Nordstrom BL, Luo W, Landis SH, Shantakumar S. Incidence of new–onset hypertension in cancer patients: a retrospective cohort study. Int J Hypertens. 2013;2013:379252.
14. Barone BB, Yeh H–C, Snyder CF, Peairs KS, Stein KB, Derr RL, et al. Long–term all–cause mortality in cancer patients with preexisting diabetes mellitus: a systematic review and meta–analysis. JAMA. 2008;300(23):2754–64.
15. Cheung CY, Ma MKM, Chak WL, Tang SCW. Cancer risk in patients with diabetic nephropathy: A retrospective cohort study in Hong Kong. Medicine. 2017;96(38):e8077.
16. Vajdic CM, McDonald SP, McCredie MR, van Leeuwen MT, Stewart JH, Law M, et al. Cancer incidence before and after kidney transplantation. JAMA. 2006;296(23):2823–31.
17. Butler AM, Olshan AF, Kshirsagar AV, Edwards JK, Nielsen ME, Wheeler SB, et al. Cancer incidence among US Medicare ESRD patients receiving hemodialysis, 1996–2009. Am J Kidney Dis. 2015;65(5):763–72.
18. Lin HF, Li YH, Wang CH, Chou CL, Kuo DJ, Fang TC. Increased risk of cancer in chronic dialysis patients: a population–based cohort study in Taiwan. Nephrol Dial Transplant. 2012;27(4):1585–90.
19. Béchade C, Dejardin O, Bara S, Bouvier V, Guizard A–V, De Mil R, et al. Incidence and characteristics of chronic renal replacement therapy in patients with cancer: data from kidney and cancer registries in Basse–Normandie. Journal of nephrology. 2018;31(1):111–8.
20. Stengel B. Chronic kidney disease and cancer: a troubling connection. J Nephrol. 2010;23(3):253–62.
21. Małyszko J, Kozlowski L, Kozłowska K, Małyszko M, Małyszko J. Cancer and the kidney: dangereoux liasons or price paid for the progress in medicine? Oncotarget. 2017;8(39):66601–19.
22. Holley JL. Screening, diagnosis, and treatment of cancer in long–term dialysis patients. Clin J Am Soc Nephrol. 2007;2(3):604–10.
23. Oneschuk D, Fainsinger R. Medical and ethical dilemmas when an advanced cancer patient discontinues dialysis. Journal of palliative care. 2002;18(2):123–6.
24. Hayakawa K, Matsumoto M, Aoyagi T, Miyaji K, Hata M. Prostate cancer with multiple lung metastases in a hemodialysis patient. Int J Urol. 2000;7(12):464–6.

25. Cengiz K. Increased incidence of neoplasia in chronic renal failure (20–year experience). International urology and nephrology. 2002;33(1):121–6.

26. Castellanos M, Varma S, Ahern K, Grosso SJ, Buchbinder S, D'Angelo D, et al. Increased breast calcifications in women with ESRD on dialysis: implications for breast cancer screening. Am J Kidney Dis. 2006;48(2):301–6.

27. Coppolino G, Bolignano D, Rivoli L, Mazza G, Presta P, Fuiano G. Tumour markers and kidney function: a systematic review. BioMed research international. 2014;2014:647541.

28. Miller KD, Nogueira L, Mariotto AB, Rowland JH, Yabroff KR, Alfano CM, et al. Cancer treatment and survivorship statistics, 2019. CA: a cancer journal for clinicians. 2019;69(5):363–85.

29. Smith TG, Troeschel AN, Castro KM, Arora NK, Stein K, Lipscomb J, et al. Perceptions of Patients With Breast and Colon Cancer of the Management of Cancer–Related Pain, Fatigue, and Emotional Distress in Community Oncology. Journal of clinical oncology : official journal of the American Society of Clinical Oncology. 2019;37(19):1666–76.

30. Levey AS, Stevens LA, Schmid CH, Zhang YL, Castro AF, 3rd, Feldman HI, et al. A new equation to estimate glomerular filtration rate. Ann Intern Med. 2009;150(9):604–12.