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Original Article

Renal Insufficiency in Cancer Patients and Associated Demographic, Clinical and Treatment Characteristics at Kenyatta National Hospital, Nairobi, Kenya

Gabriel Dokata Qalicha, MBChB[1], Dr. Wangari Beatrice, MMed[1] & Dr. Namasaka Philemon, MMed[1]*

[1] Jomo Kenyatta University of Agriculture and Technology, P. O. Box 62000-00200 Nairobi, Kenya.
*Author for Correspondence ORCID ID: https://orcid.org/0009-0009-8262-483X; Email: gabrieldokqalicha@gmail.com

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ABSTRACT

Renal insufficiency is sub-optimal kidney function, affecting approximately 10% of the world population. In sub-Saharan Africa, it is approximated at 14% of the population whereas the kidney disease burden in Kenya is estimated to be at 4%. Studies show that at least 27.1% of cancer patients are suffering from renal insufficiency and need some chemotherapeutic drug adjustment. The objective of this study was to establish the prevalence of renal insufficiency and the associated clinical, demographic and treatment factors among cancer patients at KNH. A cross-sectional study where data was collected using a structured interviewer-administered questionnaire and hospital records. Systematic random sampling without replacement was used to select eligible 330 participants (patients) from Oncology wards and clinics at KNH. The information from the questionnaires was entered into a computer, cleaned, coded and loaded into R version 4.1.2 statistical software for analysis. Calculation of estimated GFR was done by CKD-Epi in micromole/l using a medical calculator to diagnose renal insufficiency and classify accordingly. The data was analyzed using both descriptive and bivariate/ multivariate regression analysis. All p-values were two-sided and the results were considered statistically significant at $p < 0.05$. A total of 56.1% were females and others were male. Of the 330 study participants, 42.7% were aged between 41-60, 41.5% above 60 years and the rest below 41 years. The prevalence of renal insufficiency was 38% (95% CI 33, 44%). Age above 60 years and the use of taxanes were significantly associated with renal insufficiency before and after adjustment (p-values <0.05). In conclusion, the prevalence of renal insufficiency among patients with cancer was high in this study of which the majority had stage 2 renal failures. Patients aged above 60 years had significantly higher odds of renal insufficiency while patients on taxanes had significantly lower odds of renal insufficiency.

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INTRODUCTION

Renal insufficiency is simply compromised kidney function and can be of acute onset (acute kidney injury) or chronic kidney disease. Chronic kidney disease is defined as the presence of an abnormality in kidney structure or function persisting for more than 3 months. This includes 1 or more of the following: (1) GFR less than 90 mL/min/1.73 m2; (2) albuminuria (urine albumin ≥30 mg per 24 hours or urine albumin-to-creatinine ratio [ACR] ≥30 mg/g); (3) abnormalities in urine sediment, histology, or imaging suggestive of kidney damage; (4) renal tubular abnormality and associated electrolyte disorder; or (5) history of kidney transplantation (Ephraim et al, 2018). On the other hand, Kidney disease improving global outcome guidelines define acute kidney injury as an abrupt loss of kidney function causing a decline in glomerular filtration rate (GFR), retention of urea and creatinine and dysregulation of extracellular volume and electrolytes. It defines AKI in one or more of these three criteria: Rise in Serum Creatinine from baseline of at least 0.3mg/dl (26.5mmol/L) within 48hours or 50% higher than baseline in a week or reduction in urine output to <0.5ml/kg/hour for longer than 6hrs.

In terms of GFR kidney disease is classified into five stages, with the severest form being end-stage renal disease which requires renal replacement therapy either in the form of dialysis or renal transplantation (Webster et al., 2017). Estimation of glomerular filtration rate (GFR) in ml/min/1.73m2 is the easiest method of estimating renal compromise in a clinical setting. GFR is estimated and classified into 5 stages; G1 (≥ 90), G2 (60-89), G3a (45-59), G3b (30-44), G4 (15-29) and G5 (<15, or treated by dialysis/renal transplant). It is worth noting that in stage one(G1) GFR is normal but other markers of kidney damage as mentioned above can be present. Albumin excretion ratio (mg/24 hours) can be classified as A1< 30, A2 30-300 and A3 >300 depending on the severity.

Albuminuria of any form indicate damage to glomerular membrane charge and size selectivity and hence abnormality in the filtration capacity of the kidney. In the same vein albumin creatinine ratio in urine (mg/g) is categorized into A1< 30, A2 30-300 and lastly A3 >300 (KDIGO, 2012). AER is a sensitive and early indicator of kidney damage which should be used routinely to accurately assess renal insufficiency and monitor progress of kidney dysfunction. Urine sediment abnormalities include casts, crystals, white blood cells, red blood cells, epithelial cells and many others (Janus N et al, 2015). These normally show the presence of infectious processes, vascular kidney disease, and glomerular or tubulointerstitial pathology. The renal biopsies of patients with renal disease may show glomerular sclerosis and collapse, interstitial fibrosis, tubular fibrosis, tubular atrophy, interstitial

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infiltration, presence of cast and arteriolar hyalinosis. Kidney ultrasound can be used to assess the size, location, and shape of the kidneys and related structures, such as the ureters and bladder. Ultrasound can detect cysts, tumours, abscesses, obstructions, fluid collection, and infection within or around the kidneys.

The main objective of the study was to determine the prevalence of renal insufficiency and associated demographic, clinical and treatment factors among cancer patients at KNH. The specific objectives included in the study were: to describe the prevalence of renal insufficiency and demographic characteristics of cancer patients, assessment of the major cancer types, clinical characteristics and treatment modalities of cancer patients at Kenyatta National Hospital, Nairobi, Kenya.

MATERIALS AND METHODS

Study area

This study was conducted at Kenyatta National Hospital (KNH), the oldest and largest referral hospital in the country and East Africa. KNH has a capacity of over 2,400 beds and provides both routine and specialized medical and surgical services, along with preventive and rehabilitative healthcare. KNH was chosen for this research because it is a major national referral hospital that treats patients with cancer, renal diseases, and other health issues. Its nationwide catchment area is also expected to provide representative data and a sufficient sample size for the research activities.

Research design

A cross-sectional study design was used among oncology inpatient wards and outpatient clinics at the Kenyatta National Hospital. In this study, data was collected from inpatient ward and outpatient clinic records and interviews of individual patients.

Study population

Study participants included all adult patients, above 18 years, who were admitted to the adult oncology wards and those who attended the outpatient clinic at Kenyatta National Hospital over a period of 3 months (July–September 2024) and who met the eligibility criteria.

Inclusion criteria

All patients admitted in the Oncological wards or attending outpatient oncology clinics aged 18 years and above, who gave consent were included in the study.

Exclusion criteria

Patient with kidney disease secondary to any other cause as identified by a nephrologist (Diabetic, hypertensive, Polycystic, HIV related, glomerulonephritis related kidney diseases). Critically ill patients and patients whose urea, electrolyte and creatinine levels were not available for whatever reason

Sample size

The sample size was determined using Fischer's formula.

This was based on a previous study conducted in Turkey which found that the prevalence of renal insufficiency in cancer patients was estimated to be 27.1%.

Therefore;

$$n = \frac{Z^2 P (1-P)}{e^2} =$$

n= minimum sample size required for the study

z= 1.96 (normal z value at 95% confidence interval)

e= 0.05 (Margin of error)

P= 27.1% (estimated proportion of cancer patients having renal insufficiency)

$$n = \frac{1.96^2 * 0.271 (1-0.271)}{0.05 \times 0.05} = 304$$

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A non-response factor of 10% was added to the sample (Israel,1992)

n + 10% = 10 x 304/100 = 31

The total sample size will be 304 + 31 = 335 eligible patients.

Sampling procedures

A pre-visit was conducted before the commencement of the study to ascertain the patients admitted to the oncology ward and the average daily attendance of the outpatient oncology clinic at the time of the study. The number of participants for sampling from each ward and clinic was allocated proportionately in accordance with the capacity of each unit. Systematic random sampling was used to select eligible patients from each ward and clinic. This was carried out for a period of 3 months (July-September) until 335 participants were recruited.

Data collection tools

Data was collected using researcher-administered structured questionnaires after getting informed consent from individual patients. Information on demographic characteristics: age and gender were collected through face-to-face interviews. Data on laboratory investigation (estimated glomerular filtration rate), clinical stage and treatment modalities were obtained from patient's files.

Validity and reliability of study tools.

The questionnaire was pre-tested in a pilot study comprising 10% of the sample patients selected from ward or general medical outpatient clinic 2 weeks prior to the study (Hertzog, 2008). The population on which the instrument was tested was similar to the one that participated in the actual study.

Validity was ensured by confirming that all the questions to be asked in the questionnaire were relevant, clearly comprehensive enough to collect all information needed, represented the content and had the same meaning to all respondents. It was also established using a field test on a population not included in the sample. Changes were made as appropriate based on the field test.

Reliability was ascertained by the test-retest method (Cronbach's Alpha of 0.75) was regarded as appropriate. This was determined by administering the survey questionnaire at two different points in time to the same respondents and determining the correlation or strength of association of the two sets of scores.

Study variables

The independent variables were demographic data, clinical stage of the disease and treatment modalities. The dependent variable was renal insufficiency as measured by CKD- EPI estimated glomerular filtration rate in micromole/l

Study procedures

The researcher trained two research assistants who were going to administer questionnaires to individual patients through face-to-face interviews. The research assistants must have had at least a diploma and also knowledgeable in the field of data collection. Both oral interviews and information from the files were used to collect the required information. The researcher and the research assistants cleaned and summarized the data daily to make sure that the data collected was accurate.

Data analysis and presentation plan

Data from the questionnaires was entered into a computer, cleaned, coded and loaded into R version 4.1.2 for analysis. Calculation of GFR was done using the CKD-Epi equation to diagnose renal insufficiency. The patients were accordingly classified into five stages of renal failure using GFR in ml/min/1.73m2. Categorical variables e.g., the sex of the patients and the clinical staging of cancer were summarized using frequencies and proportions. The age of the patients in continuous form was summarized using the median and interquartile range. The proportion of the number of patients with impaired renal function out of the total number of participants in the study gave the overall

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prevalence of renal disease in cancer patients. These were then classified according to age, sex, clinical stage of the cancer and various treatment modalities using tables. The association between renal insufficiency in cancer patients and clinical stage, treatment modalities and demographic characteristics were analyzed using descriptive statistics and bivariate analysis methods. Variables with p-values of less than 0.25 were selected for the multivariable model (Bursac et al., 2008). Results were presented using p values and odds ratios.

Data quality management

To ensure appropriate data quality management, the principal investigator checked the questionnaires daily for accuracy, consistency and completeness and provided feedback and correction regarding the collected data daily to the research assistants.

Ethical considerations

Clearance was obtained from the JKUAT Scientific and Ethics Review Committee. In addition, clearance to do the research at KNH was obtained from the KNH/UON scientific and ethics review committee and also NACOSTI. Permission was also sought from the head of the oncology department and other consultants in the wards. Written informed consent was sought from each participant after explaining to them what the study involved and their cooperation requested. Patients' information was kept confidential in compliance with the Data Protection Act (2019).

RESULTS AND DISCUSSION

Demographic characteristics of the patients

This study included a total of 330 patients (98.5% of total participants of 335). Five patients whose data was not complete were left out of the analysis. Out of the 330 patients, 185 (56.1%) were females and the rest were males. A total of 141 (42.7%) were aged between 41-60 years, 137 (41.5%) were above 60 years and the rest were below 40 years as shown in the Table below.

Table 1: Demographic characteristics of the patients (n = 330)

Variable	Frequency	Percent (%)
Gender		
Male	145	43.9
Female	185	56.1
Age in years		
Median age (IQR): 57 (45,67)		
≤40	52	15.8
41-60	141	42.7
>60	137	41.5

Cancer diagnosis and clinical staging

Organ involved

The study tackled renal insufficiency among five major cancers treated at KNH. The number of participants for individual cancer is shown below in Figure 1.

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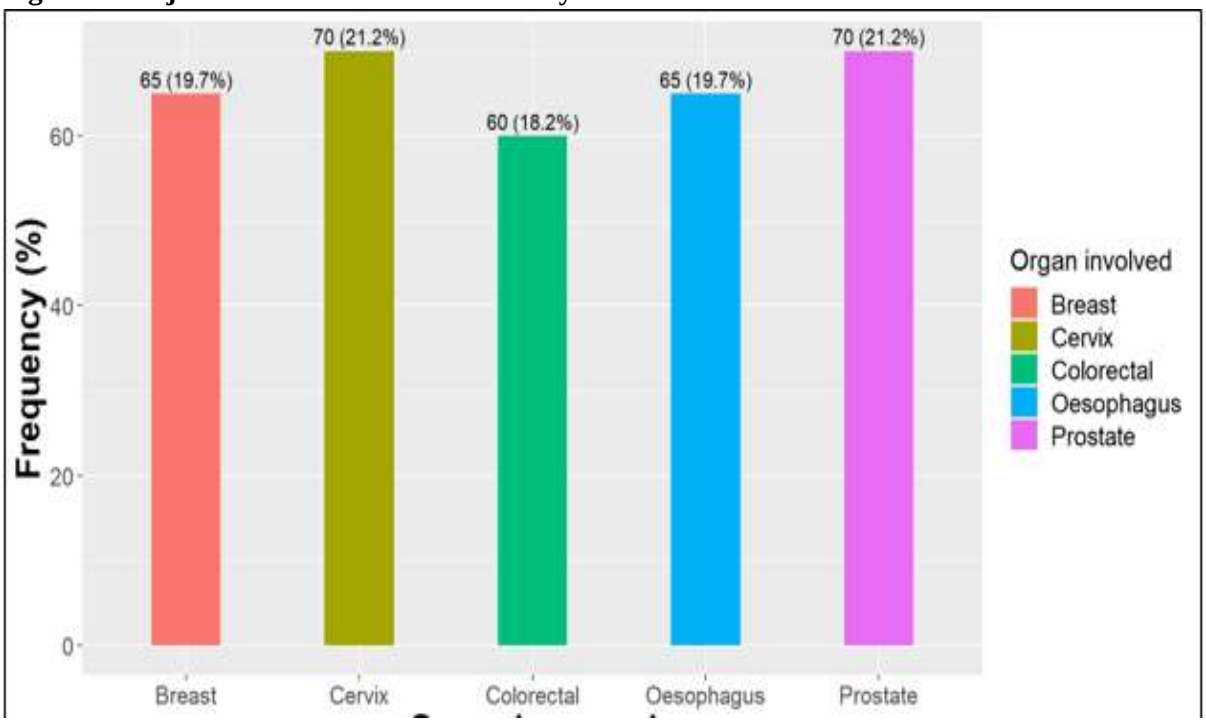
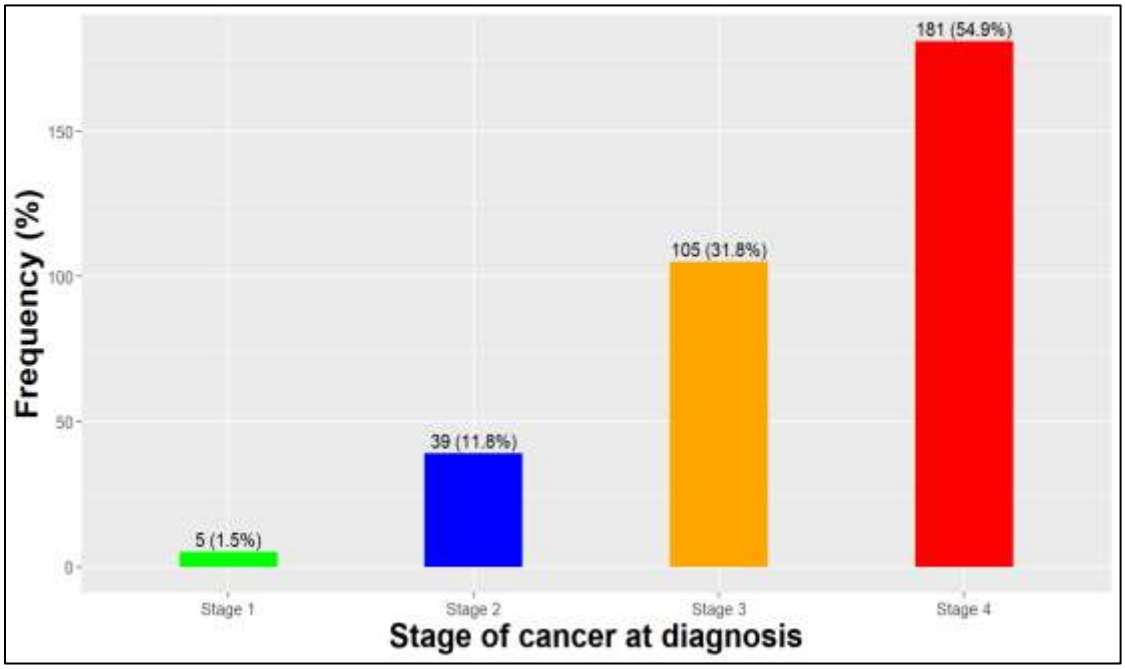
Figure 1: Major cancers involved in the study



Stage of cancer at diagnosis

Most of the patients who took part in this study were either diagnosed in stage 3 or 4 of the disease with only 5 patients diagnosed at stage 1 as shown in the figure below.

Figure 2: Stage of cancer at diagnosis



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Stages of cancer diagnosis based on the organ involved

All the five cancers involved in the study had similar stages at the time of diagnosis. Only 2 patients with cervical cancer and 3 patients with colorectal cancer were diagnosed in stage 1. The majority of the patients were diagnosed in stages 3 and 4 as shown in Table 2 below.

Table 2: Stage of cancer diagnosis and the affected organ

Organ involved	Stage 1 n (%)	Stage 2 n (%)	Stage 3 n (%)	Stage 4 n (%)	Total
Breast (n = 65)		7	11 (16.9%)	47 (72.3%)	65 (100%)
Cervix (n = 70)	2	7	32 (45.7%)	29 (41.4%)	70 (100%)
Colorectal (n = 60)	3	5	21 (35%)	31 (71.7%)	60 (100%)
Oesophagus (n = 65)		11 (16.9%)	33 (50.8%)	21 (32.3%)	65 (100%)
Prostate (n = 70)		9	8	53 (75.7%)	70 (100%)
Total	5	39 (11.8%)	105 (31.8%)	181 (54.9%)	330 (100%)

Cancer Management modalities

Out of the 330 patients, 296 (89.7%) were on cancer treatment while the rest were not. Of the 34 patients who were not on treatment, 29 (85.3%) were still to finalize baseline workup for cancer diagnosis and staging while the remaining five were waiting for stabilization because they were too weak to start treatment. Different treatment modalities used are shown in the figure below.

Table 3: Cancer management modalities

Management modality	Frequency (%)
Already on cancer treatment	
Yes	296 (89.7%)
No	34 (10.3%)
Reasons why not on cancer treatment (n = 34)	
Not yet finalize baseline workup	29 (85.3%)
Too weak to start, waiting for stabilization	5 (14.7%)
Those already on cancer treatment	
Chemotherapy	
Platinum (*carboplatin, cisplatin, oxaliplatin*)	130 (39.4%)
Taxanes (*Paclitaxel, docetaxel*)	68 (20.6%)
Antimetabolites (*Capecitabine, gemcitabine, fluorouracil)*	52 (15.8%)
Others (*etoposide, irinotecan, vincristine, cyclophosphamide, adriamycin*)	16 (4.8%)
Surgery	152 (46.1%)
Reasons for surgery	
Palliative	25 (16.5%)
Tumor staging	75 (49.3%)
Tumor removal	52 (34.2%)
Radiotherapy	126 (38.2%)
Immunotherapy	40 (12.1%)
Hormonal therapy	
Goserelin	58 (17.6%)
Abiraterone	29 (8.8%)
Letrazole/anstrazole	7 (2.1%)
Others (fulvestrant, tamoxifen, bicalutamide/casodex)	10 3%)

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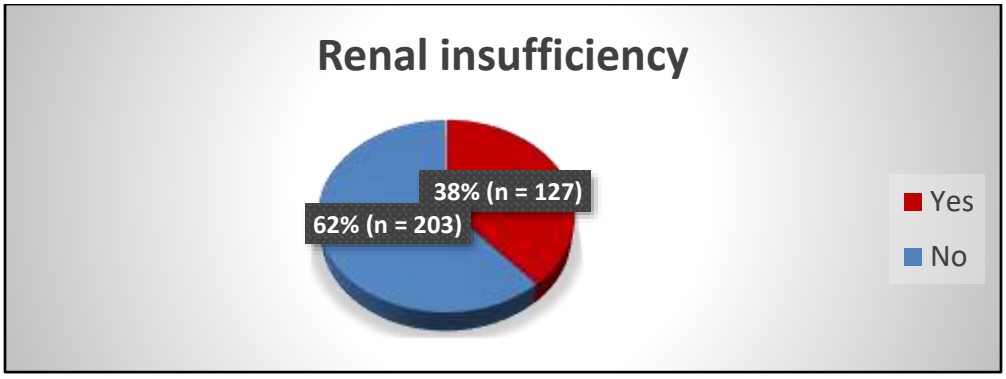
The prevalence of renal insufficiency among cancer patients

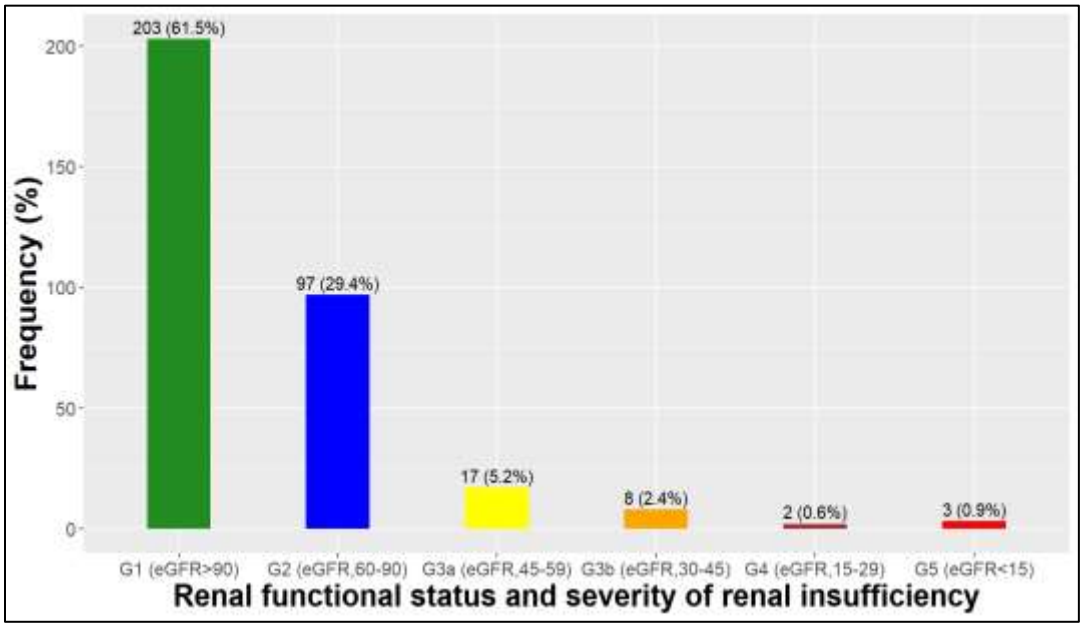
Patients with renal insufficiency were defined as those with an estimated GFR of 89 mL/min/1.73 m2 and below. There were 127 patients in this category giving us a prevalence of 38% (95% CI 33%, 44%) as shown.



Renal functional status and severity of renal insufficiency among cancer patients

In terms of renal function status and severity, the majority of the patients, 203 (61.5%) had normal renal function (eGFR>90). A total of 97 (29.4%) had mild renal failure (eGFR 61-89). Those with moderate stage G3a (eGFR 45-59) were 17 (5.2%), and stage G3b (eGFR 30-44) were 8 (2.4%). The rest is shown in Figure 4.

Figure 4: Renal functional status and severity of renal insufficiency among cancer patients



Factors associated with renal insufficiency among patients treated with cancer

From the analysis, two factors (age >60 years and the use of taxanes) were significantly associated with renal insufficiency under bivariate analysis (p values <0.05) at a 5% significance level. Patients above the age of 60 were 2.16 times more likely to have renal insufficiency compared to patients aged 40 years and below, OR 2.16 (95% CI 1.10, 4.35).

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Patients on taxanes had 54% lower odds of renal insufficiency compared to those who were not on taxanes, OR 0.46 (95% CI 0.25, 0.83).

Other factors that increased the odds of renal insufficiency though they were not statistically significant were; the type of cancer when compared to breast cancer and being on letrazole among others. The odds of renal insufficiency were 97% higher among patients with cervical cancer compared to patients with breast cancer, OR 1.97 (95% CI 0.99, 4.00). The patients with colorectal cancer had 13% higher odds of renal insufficiency compared to those with breast cancer, OR 1.13 (95% CI 0.53, 2.38). Patients who were treated with letrozole had 4.12 times higher odds compared to those who were not on letrozole OR 4.12 (95% CI 0.87, 29.07).

After adjustment, age above 60 years and treatment with taxanes remained significantly associated with renal insufficiency (p-values<0.05). Patients aged above 60 years were 2.33 times more likely to develop renal insufficiency compared to those aged 40 years and below, aOR 2.33 (95% CI 1.16, 4.87). Patients put on taxanes were 53% less likely to develop renal insufficiency compared to those not on taxanes, aOR 0.47 (95% CI 0.25, 0.85) as shown in Table 4.

Table 4: Factors associated with renal insufficiency among patients treated with cancer

Factors	Renal sufficiency					
Demographic characteristics	**Yes n = 127**	**No n = 203**	**cOR (95% CI)**	**P-value**	**aOR (95% CI)**	**p-value**
Gender						
Female	70	115	0.94 (0.60, 1.47)	0.785		
Male	57	88	***Reference***			
Age in years						
≤40	15	37	***Reference***			
41-60	48	93	1.27 (0.65, 2.63)	0.495	1.38 (0.68, 2.89)	0.384
>60	64	73	2.16 (1.10, 4.35)	**0.028**	2.33 (1.16, 4.87)	**0.020**
Cancer Characteristics						
Cancer type						
Breast	21	44	***Reference***			
Cervix	34	36	1.97 (0.99, 4.00)	0.056		
Colorectal	21	39	1.13 (0.53, 2.38)	0.750		
Esophagus	23	42	1.15 (0.56, 2.38)	0.711		
Prostate	28	42	1.39 (0.69, 2.86)	0.354		
Cancer histology						
Adenocarcinoma	55	94	***Reference***			
Ductal carcinoma	21	43	0.83 (0.44, 1.54)	0.567		
Neuroendocrine	2	2	1.71 (0.20, 14.29)	0.597		
Squamous cell	49	64	1.31 (0.79, 2.17)	0.291		
Cancer stage						
Stage 1	2	3	***Reference***			
Stage 2	14	5	0.84 (0.12, 7.14)	0.858		
Stage 3	39	66	0.88 (0.14, 7.14)	0.897		
Stage 4	72	109	0.99 (0.16, 7.69)	0.992		

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Factors	Renal sufficiency					
Demographic characteristics	**Yes n = 127**	**No n = 203**	**cOR (95% CI)**	**P-value**	**aOR (95% CI)**	**p-value**
Treatment modalities						
On treatment						
Yes	112	184	0.77 (0.38, 1.61)	0.477		
No	15	19	***Reference***			
Surgery						
Yes	62	90	1.31 (0.82, 2.10)	0.263		
No	50	95	***Reference***			
Radiotherapy						
Yes	47	79	0.97 (0.60, 1.56)	0.901		
No	65	106	***Reference***			
Immunotherapy						
Yes	28	12	0.67 (0.32, 1.36)	0.282		
No	157	100	***Reference***			
Chemotherapy						
Platinum derivatives						
Yes	53	77	1.17 (0.74, 1.84)	0.492		
No	74	126	***Reference***			
Taxanes						
Yes	17	51	0.46 (0.25, 0.83)	**0.012**	0.47 (0.25, 0.85)	**0.015**
No	110	152	***Reference***			
Antimetabolites						
Yes	21	31	1.10 (0.60, 2.00)	0.759		
No	106	172	***Reference***			
Others (etoposide, irinotecan, vincristine, cyclophosphamide, adriamycin**)**						
Yes	4	12	0.52 (0.14, 1.52)	0.263		
No	123	191	***Reference***			
Hormonal therapy						
Goserelin						
Yes	23	35	1.06 (0.59, 1.89)	0.840		
No	104	168	***Reference***			
Abiraterone						
Yes	9	20	0.70 (0.29, 1.54)	0.390		
No	118	183	***Reference***			
Letrazole/anastrazole						
Yes	5	2	4.12 (0.87, 29.07)	0.094	4.81 (0.99, 34.65)	0.067
No	122	201	***Reference***			
Others (fulvestrant, tamoxifen, bicalutamide)						
Yes	2	8	0.39 (0.06, 1.59)	0.239		
No	125	195	***Reference***			

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DISCUSSION

The current study showed that renal insufficiency was high [(38%), 95% CI 33-44%] among patients on cancer treatment at Kenyatta National Hospital (KNH). Literature has shown that renal insufficiency is more prevalent among patients with cancer compared to the general population (Launay-Vacher, 2010; Launay-Vacher et al., 2016). A higher prevalence of renal failure has been reported compared to the current study. For example, Rajabu et al. (2024) in Tanzania reported a prevalence of 62.2% which is way higher than what this study has reported. The two studies had similar population characteristics in terms of age distribution. Advanced ages are associated with more cases of renal failure. The differences in the two findings might have been caused by differences in the duration of cancer treatment which we did not study. Renal failure has been reported to increase with an increase in the number of years after diagnosis (Silva et al., 2018). Other studies that have reported a higher prevalence of renal insufficiency compared to the current study are Janus et al. (2010), Launay-Vacher et al. (2007) and Pontes et al. (2014).

Dogan et al. (2015) reported a renal insufficiency prevalence of 27.1%. This finding is significantly lower than that reported in the current study. This difference could be attributed to differences in the diversity of cancers studied. That study involved various types of cancers in a sample of 1217 patients. Similar to the current study, Manyau et al. (2021) in Zimbabwe reported a renal insufficiency prevalence of 43.1% among patients with breast cancer. All these findings show that renal insufficiency is highly prevalent among patients on cancer treatment.

Our study found two factors (age and the use of taxanes) to be associated with renal insufficiency among patients with cancer. Patients aged above 60 years had significantly higher odds of renal insufficiency compared to those aged 40 years and below. The higher odds of renal insufficiency among older patients are due to a decrease in renal function with an increase in age (Aapro & Launay-Vacher, 2012). This finding has been corroborated by Rajabu et al. (2024) where elderly patients had 1.4 higher odds of renal insufficiency. Our finding is also consistent with other studies conducted in the USA and Belgium, which also found that age was linked to the occurrence of renal insufficiency in cancer patients (Janus et al., 2010; Strati et al., 2017). Our study also found the use of taxanes to be significantly associated with lower odds of renal insufficiency. Contrary to our findings, chemotherapy has been associated with higher odds of renal insufficiency (Lameire, 2013). The difference in the two studies could be due to the drug studied. While our study looked specifically at taxanes, the cited study looked at chemotherapy in general hence the differences. The drug letrazole was associated with higher odds of renal insufficiency in the current study though it was not significant. Some studies have reported renal toxicity, noting that letrozole administration causes biochemical changes that disrupt tyrosine phosphorylation, which in turn affects kidney function (Puri et al., 2020) though other studies have suggested that dose adjustment is not required as the drug is tolerated even in ARF (Bednarek et al., 2020).

While our results did not show associations between type of cancer and renal insufficiency, patients with breast cancer had lower odds of renal insufficiency compared to those with oesophageal, prostate, cervical and colorectal cancers. In cancer patients, postrenal causes of AKI are more common than in the general population and should always be considered. Obstruction of the urogenital system is particularly frequent in cases of uterine, prostate, and cervical cancers. Obstruction in the urinary system can result from stone formation or clots, often seen in patients with malignancies. Ureteral obstruction may occur due to stones or external compression, while bladder outlet obstructions and tumours also lead to obstructive uropathy (Habas et al., 2023). Based on this, cancers close to the

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kidneys can be considered the highest culprits in renal failure.

Limitations

This is a single-centre study and therefore the findings cannot be generalised to other centres. The study is conducted at a national referral hospital in a major city. Therefore, the findings may not be representative of what is happening in the rural countryside.

CONCLUSION

The prevalence of renal insufficiency among patients with cancer was high in this study. The study found that renal failure was more common in cervical cancer patients compared to other types of cancers although it is not statistically significant(p=0.056). The majority of the patients with renal insufficiency had stage 2 renal failures whereas the majority of the patients were diagnosed with stage 4 cancers. Lastly, the study found that patients above 60 years had significantly higher odds of renal insufficiency while patients on taxanes had significantly lower odds of renal insufficiency compared to other forms of chemotherapeutics agents.

Recommendations

We recommend a comparison of different forms of taxane: paclitaxel, docetaxel and their relationship with renal insufficiency in future studies. Cervical cancer was found to be more associated with renal insufficiency than other cancers although it was not statistically significant(p=0.056). This finding needs to be substantiated more in future studies. We recommend a prospective longitudinal study where cancer patients of normal kidney functions were recruited and followed up to determine the prevalence of renal insufficiency in cancer patients and describe similarities and differences based on demographic features of patients, clinical characteristics and different treatment modalities patients were on at different periods of time.

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Data availability

On reasonable request, the datasets will be made available to the interested party.

Conflicts of interest

The authors declare no conflicts of interest before and during the research.

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