PREVALENCE OF RENAL INSUFFICIENCY IN PATIENTS WITH MAJOR CANCERS AND ASSOCIATED FACTORS AT KENYATTA NATIONAL HOSPITAL, NAIROBI, KENYA

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Prevalence of Renal Insufficiency in Patients with Major Cancers and Associated Factors at Kenyatta National Hospital, Nairobi, Kenya

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DECLARATION

This thesis is my original work and has not been presented for a degree in any other University

Signature…… Date…….....

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This thesis has been submitted for examination with our approval as the University Supervisors

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DEDICATION

I dedicate this thesis to my Dear wife, Sarah Midina Galgallo for the support she gave me during my studies.

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I wish to start by thanking the Almighty God for His grace. He has guided me as far as this Thesis is concerned. Secondly, I wish to convey my gratitude to Jomo Kenyatta University of Agriculture and technology in general, School of Medicine in particular for giving me chance to pursue my masters at the School.

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ACRONYMS AND ABBREVIATIONS

ACR	Albumin Creatinine Ratio
AER	Albumin Excretion Ratio
AIDS	Acquired Immunodeficiency Syndrome
AJCC	American Joint Committee on Cancer
AKI	Acute Kidney Injury
CKD	Chronic Kidney Disease
GFR	Glomerular Filtration Rate
GOK	Government of Kenya
HIV	Human Immunodeficiency Virus
ICI	Immune Checkpoint Inhibitors
KDIGO	Kidney Disease Improving Global Outcome
KDOQI	Kidney Disease Outcome Quality Initiative
KFRT	Kidney Failure Requiring Replacement Therapy
KNH	Kenyatta National Hospital
MOK	Ministry of Health
NACOSTI	National Commission for Science, Technology and Innovation.
NSAIDs	Non-Steroidal Anti-Inflammatory Drugs

RCC	Renal Cell Carcinoma
RI	Renal Insufficiency
TLS	Tumor lysis Syndrome
UICC	Union for International Cancer control
WHO	World Health Organization

DEFINITIONS OF OPERATIONAL TERMS

Acute kidney injury Reduction in the efficiency of kidney function leading to the accumulation of metabolic waste product in blood including urea and creatinine normally lasting less than 3 months. AKI can come as result of compromised circulatory volume, pathologies affecting the kidney parenchyma or post renal obstruction. Regardless of possible pathologies eGFR of less than 90 mL/min/1.73 m2 was used to classify presence and severity kidney disease in this study.

Chronic kidney disease (CKD) 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 (ie, 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 disorders; or (5) history of kidney transplantation. Because this is cross sectional study and differentiating above two may be difficult, estimated glomerular filtration rate is solely used to classify extent of renal impairment in this study. As stated above eGFR of less than 90 mL/min/1.73 m2 was used to classify presence and severity kidney disease in this study.

Proteinuria In this study participant with proteinuria positive in urine dipstick or albuminuria (urine albumin ≥30 mg per 24 hours or urine albumin-to-creatinine ratio [ACR] ≥30 mg/g) were regarded as having proteinuria; Proteinuria is pathological finding indicating damage in filtrating glomerular membrane.

Renal insufficiency Means compromised kidney functions as indicated by increased urea and creatinine levels in blood. Reduced kidney function can be of acute onset (acute kidney injury) or chronic kidney disease depending on the duration of

pathology. In this study estimated GFR of less than 90 mL/min/1.73 m2 as measured by CKD- EPI medical calculator in micromole/ l was considered as renal insufficiency.

ABSTRACT

Renal insufficiency, defined as a reduction in kidney function, represents a major global health challenge, affecting about 10% of the world's population. In sub-Saharan Africa, the burden is estimated at 14%, while Kenya reports a prevalence of approximately 4% in the general population. Among cancer patients, earlier studies indicate that up to 27.1% experience renal insufficiency, often necessitating chemotherapy dose adjustments. This study aimed to determine the prevalence of renal insufficiency and identify associated demographic, clinical, and treatment-related factors among cancer patients receiving care at Kenyatta National Hospital. A cross-sectional study design was employed, involving 335 systematically selected oncology patients from KNH wards and clinics. Data were collected through structured interviewer-administered questionnaires and review of hospital records. After exclusion of five participants due to incomplete data, 330 patient records were analyzed. Data entry, cleaning, and analysis were conducted using R (version 4.1.2). Estimated glomerular filtration rate (eGFR) was calculated using the CKD-EPI micromole/L calculator to diagnose and stage renal insufficiency. Descriptive statistics summarized patient characteristics, while associations between renal insufficiency and demographic, clinical, and treatment variables were assessed using bivariate and multivariable logistic regression. Statistical significance was set at $p<0.05$. Among the 330 participants, 56.1% were female. Most patients were aged 41–60 years (42.7%), followed closely by those above 60 years (41.5%). The overall prevalence of renal insufficiency was high at **38%** (95% CI: 33–44%). Majority of patients had mild renal impairment (eGFR 61–89 mL/min/1.73 m²) accounting for 29.4% of cases whereas severe stages were less common, with stage 4 observed in (2)0.6% and stage 5 in (3)0.9% of patients. Multivariable logistic regression revealed two significant associations. Patients older than 60 years had a more than two-fold higher likelihood of renal insufficiency (AOR=2.33; 95% CI: 1.16–4.87; p=0.020). Conversely, the use of taxane-based chemotherapy was associated with a lower prevalence of renal insufficiency (AOR=0.47; 95% CI: 0.25–0.85; p=0.015). The study concludes that renal insufficiency is common among cancer patients at KNH, with advanced age posing a significant risk. Close monitoring of renal function, especially in elderly patients undergoing cancer treatment, is strongly recommended.

CHAPTER ONE

INTRODUCTION

1.1 Background to the Study

Renal insufficiency is defined as 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 (that is, urine albumin excretion ratio of ≥30 mg in 24 hours or urine albumin-to-creatinine ratio [ACR] ≥30 mg/g or ≥3mg/mmol); (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). 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, Nagler, Morton & Masson, 2017). Estimation of glomerular filtration rate (GFR) in ml/min/1.73m2 is easiest method of estimating renal compromise in 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. The same can be measured in albumin- creatinine ratio as A1< 30mg/g (3mg/mmol), A2 30- 300mg/g (3-29mg/mmol) and A3 >300mg/g (>30mg/mmol), KDIGO, 2012. Albuminuria of any form indicate damage to glomerular membrane charge and size selectivity and hence abnormality in the filtration capacity of the kidney. AER is sensitive and early indicator of kidney damage which should be used routinely to accurately assess renal insufficiency and monitor progress of kidney dysfunction. Urine sediments abnormalities include casts, crystals, white blood cells, red blood cells, epithelial cells and many others (Janus et al, 2015). These normally show presence of

infectious process, vascular kidney disease, glomerular or tubulo-interstitial pathology. The renal biopsies of patients with renal disease may show glomerular sclerosis and collapse, interstitial fibrosis, tubular fibrosis, tubular atrophy, interstitial 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, tumors, abscesses, obstructions, fluid collection, and infection within or around the kidneys. The figure below shows GFR and levels of albuminuria as predictor of kidney damage and prognosis in chronic kidney disease according to Kidney disease: improving global outcomes (KDIGO), 2012 guidelines

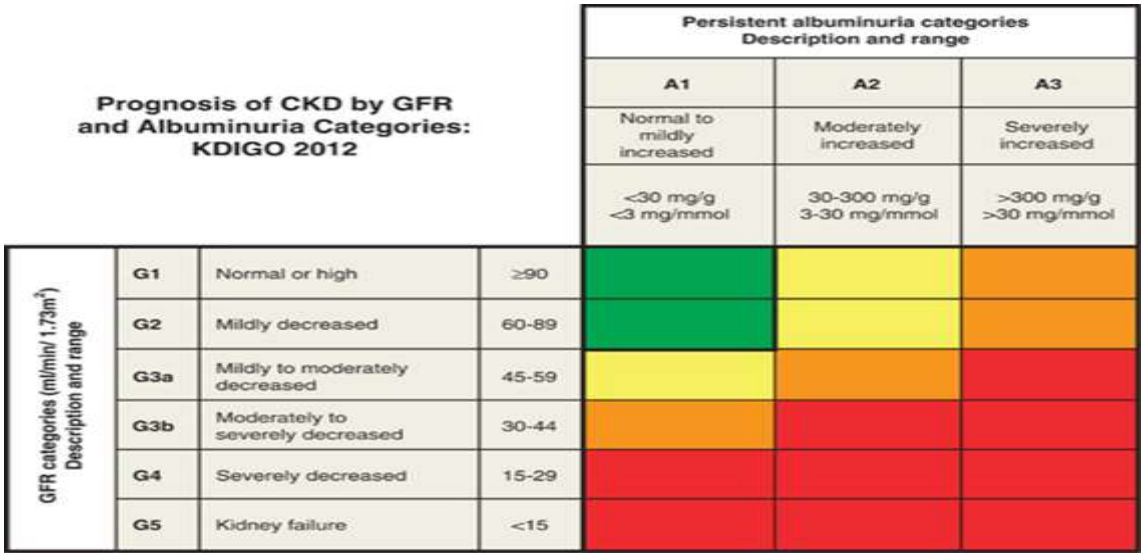

Figure 1.1: Prognosis of CKD by GFR and Albuminuria Categories

Source: Adapted and redrawn from KDIGO 2012 Clinical Practice Guideline. Original figure © KDIGO

Key
Green: low risk (if no other markers of kidney disease, no CKD)
Yellow: moderately increased risk
Orange: high risk
Red: very high risk

Kidney disease improving global outcome guideline 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.

Causes can be pre renal where severe volume loss and obstruction in renal arteries cause severe hypoxic death of renal cells. Acute kidney disease and poisoning is another important cause of kidney dysfunction. Lastly obstruction in the renal pelvis, ureter, bladder or urethra can completely block urine flow causing hydronephrosis which has detrimental effects on kidney function unless timely removal of offending factor is done. AKI can be reversed with adequate hydration or removing the offending factor. A dialysis may be needed in case of severe reduction in GFR to alleviate severe systemic complications and death. However, there is increase in incidence of such patients developing chronic kidney disease later on in life (Dogan et al., 2015). The figure below classifies stage of acute kidney injury depending on urine out-put changes and creatinine level.

Table 1.1: KDIGO Staging of Acute Kidney Injury

Stage	Serum creatinine	Urine output
1	1.5-1.9×baseline or ≥0.3 mg/dl (≥26.5 mmol/l) increase	<0.5 ml/kg/h for 6-12 h
2	2.0-2.9×baseline	<0.5 ml/kg/h for >12 h
3	3.0×baseline, or increase in serum creatinine ≥4.0 mg/dl (≥353.6 mmol/l), or initiation of RRT, or decrease in eGFR <35 ml/min/1.73 m² for patients <18 years	<0.3 ml/kg/h for ≥24 h or anuria for ≥12 h

KDIGO: Kidney disease: Improving global outcomes; RRT: Renal replacement therapy; eGFR: Estimated glomerular filtration rate

The glomerular filtration rate category (G1-G5) is used to categorize the state of renal functionality regardless of whether it is of acute or chronic onset since differentiating the two is difficult in this cross-sectional study.

Most cancers are known to affect kidney function as a complication. Renal insufficiency is one of the major comorbidities in cancer patients worsening the cancer prognosis. Such cancers include those cancers originating from kidney tissue like renal cell carcinoma or from any other tissues and organ like cervix, breast, lung, stomach, colon, prostate, multiple myeloma, leukemia and many others. The global burden of chronic kidney disease is estimated to be 11 to 13% (Hill et al., 2016). The prevalence of renal disease in African is substantial especially in the middle-aged people in sub- Sahara Africa and approximated at 14% whereas kidney disease burden in Kenya it is estimated to be at 4% in general population (Naicker, 2017). A cross-sectional study of 306 medical inpatients at Kenyatta National Hospital found that 38.6% (118 patients) had CKD (Mwenda et al, 2019).

Kidney dysfunction in oncology patients has detrimental impact on their treatment and quality of life. Patients suffering from cancer have a significantly higher prevalence of chronic kidney disease compared to the general population, dependent of the age of the patients and the type of cancer. A Study done in Turkey (Dogan et al, 2015) showed that at least 27.1% of cancer patients are suffering from renal insufficiency and need some chemotherapeutic drugs adjustment. Direct invasion of the urinary system or distant metastasis, repeated aggressive and potential nephrotoxic therapeutic interventions, malnutrition, hyperuricemia, paraneoplastic syndrome involving the kidney all increases chances of renal disease. Any pathology affecting arterioles, glomerular surface and basement membrane, bowman capsule and tubular structures reduces net filtration, hence compromising kidney function.

A study done in France on the renal insufficiency and cancer medication administration (IRMA) showed that a total of 50–60% of the 4684 cancer patients had abnormal renal function (GFR<90), whereas SCR levels were normal in most patients (Launay-Vacher et al, 2016). These findings emphasize the high incidence of RI in cancer patients. This is an important issue in clinical practice for the handling of anticancer drugs and close monitoring of renal dysfunction in those patients. As approximately 50% of all anticancer drugs are excreted predominantly in the urine as unchanged drug or active metabolite

(Booth & Morley, 2019). Any reduction in renal clearance can result in accumulation of potentially toxic species and over dosage. The dosage of chemotherapeutic agents used in patients with renal insufficiency thus frequently requires dosage reduction to avoid severe toxicity. A study done in the Côte d'Ivoire (Yao et al., 2017), found the prevalence of renal failure among cancer patients at 49%. Out of 267 total cancer patients 131 were found to have renal failure. In East Africa a study by Rajabu, Hinderaker, Mnandi & Mutagonda (2024) on prevalence of renal insufficiency among selected cancer patients on chemotherapy at Ocean Road Cancer Institute, Tanzania, 62.2% of patients on chemotherapy had renal insufficiency (by creatinine clearance). However, locally in Kenya there is no comprehensive study that looked into the prevalence of renal insufficiency in cancer patients as well as patients on different treatment modalities for treating cancer.

Acute kidney injury (AKI) and electrolyte disturbances are the most common forms of renal disease that may occur in a hospitalized patient with cancer. Important factors potentiating AKI in these patients are extracellular volume depletion due to vomiting, diarrhea, urinary tract obstruction, fluid and electrolyte disturbances, exposure to contrast media, nephrotoxic antibiotics, non-steroidal anti-inflammatory drugs and nephrotoxicity of some of the anti-cancer treatments (Wong et al., 2019; Ismail et al., 2019).

1.2 Statement of the Problem

Renal insufficiency is common in cancer patients. The evidence clearly demostrate that, when patients with cancer develop acute or chronic kidney disease, outcomes are inferior, and the promise of curative therapeutic regimens is lessened as demonstrated by work done by other author (Dogan et al, 2015). As mentioned above there was no adequate study in the local settings on prevalence of renal insufficiency in various types of cancers as well as patients already on different treatment modalities. Additionally, there were no enough literatures in the local setting on the relationship between clinical and demographic characteristic and renal insufficiency in cancer patients. Against the above

background, therefore, the current study was designed to assess renal insufficiency and associated clinical, demographic and treatment modalities of major cancers at KNH.

1.3 Justification of the Study

Renal compromise has been known to be one of the common complications, contributing to morbidity and mortality of various types of malignancies. However, there was no adequate study in the country to substantiate this general assumption. This study can shade more light on prevalence of renal disease in patients managed for 5 major cancers (Macharia, Mureithi & Omu, 2018). We limited study to the five major cancers because they represent the largest proportion of our patient population and provide adequate sample sizes for meaningful statistical analysis to ensures more reliable, interpretable, and clinically applicable findings regarding renal insufficiency. It can also help whether clinical staging of cancers and demographic characteristics of patients increase the risk of renal insufficiency. The Study investigated possible risk factors for renal dysfunction in cancer patients who were treatment naïve or on various modalities of management. The study findings will support advocating for early diagnosis and prompt remedial measures in order to reduce renal related morbidity and mortality in cancer patients. This is indispensable for health care workers managing patients, healthcare administrators, government policy makers and other stakeholders in order to maximize patient care through identification of risk factors for kidney disease in cancer patients and advocating for evidenced based mitigation measures alleviating preventable morbidity and mortality. This can save lives.

1.4 Research Questions

1. What was the demographic characteristic of the cancer patients and its relationship to renal insufficiency at KNH?
2. What were the major cancer types, clinical characteristic and the association with renal insufficiency at KNH?

3. What were the main treatment modalities of cancer patients and the relationship with renal insufficiency at KNH?
4. What was the prevalence of renal insufficiency in patients with major cancers at KNH?

1.5 Objectives of the Study

1.5.1 Broad Objective

To determine the prevalence of renal insufficiency and associated demographic, clinical and treatment factors among cancer patients at KNH.

1.5.2 Specific Objectives

1. To describe the demographic characteristic of cancer patients and the relationship with renal insufficiency at KNH.
2. To assess the major cancer types, clinical characteristic and the association with renal insufficiency at KNH.
3. To describe main treatment modalities of cancer patients and the relationship with renal insufficiency at KNH.
4. To describe the prevalence of renal insufficiency in patients with major cancers at KNH.

1.6 Assumptions of the Study

The study was conducted on the assumption that the patient did not have history of kidney disease before cancer diagnosis, and had no cognitive dysfunction or extreme weakness that could make them not participate in the interview.

1.7 Scope of the Study

1. It was limited to eligible cancer patients aged more than 18 years in the oncology wards and outpatient clinic at KNH, Nairobi, Kenya. Five most common cancers: breast, prostate, esophageal, colorectal and cervical cancers were considered for the study.
2. Data were collected using inpatient and outpatient clinic medical records and interviews of individual patients.

1.8 Limitations of the Study

The study was conducted in a single hospital and this may raise concern on generalizing the study findings to the general country's population. The study was conducted at oncology wards and clinics at tertiary level 6 hospital in the city and may raise concerns on generalizing to the rural populations where most of the citizens live. This is cross-sectional study which may not differentiate whether patient was having acute kidney injury or chronic kidney disease. There are also small number of patients with the early stage of cancer who may not be referred to oncology units after surgical intervention in different wards in the hospital. However, the study enhanced generalizability through stringent sampling (stratified proportional consecutive sampling) and contextual analysis, used available clinical data to strictly classify renal dysfunction. Minimizing errors by stringent data entry and analysis and employing adequately trained data collectors.

CHAPTER TWO

LITERATURE REVIEW

2.1 Introduction

This chapter contains a review of selected literature related to the prevalence of renal insufficiency in cancer patients. It focuses on assessing renal insufficiency in various types of cancers. Major cancers covered in this study included: Cervical, esophageal, prostate, breast and colorectal. Demographic features and clinical characteristics of cancer patients were looked at. And finally assessment of renal insufficiency in treatment naïve and patients already on various treatment modalities were tackled.

2.2 Renal Insufficiency and Patient's Demographic Characteristics

2.2.1 Age

Older age has also been recognized as a risk factor for CKD in cancer patient (Falodia, 2012). One explanation is that renal function generally decreases with age; Beginning in the third decade there is physiological loss of kidney function at rate of 1ml/min/m2 per year. Reduced glomerular filtration rate with age predisposes individuals to renal insufficiency in case of underlying cancers. Report on renal insufficiency in elderly cancer patients: International Society of Geriatric Oncology clinical practice recommendations (2018) noted that elderly cancer patients commonly have renal function decline. This warrants particular caution during the administration of renally excreted cancer drugs or those with established nephrotoxicity. Another study **(**Stuart et al, 2016) also reinforced above: by the age of 70, renal function had declined by 40%. This reduction in glomerular filtration rate (GFR) may lead to enhanced toxicity of drugs, particularly those with significant renal excretion, such as cisplatin, carboplatin, topotecan, methotrexate and ifosfamide. Because aging is highly individualized, the best guide to treatment of the older patient with cancer may be provided by a comprehensive assessment that evaluates such diverse areas as functional status, comorbidity, socioeconomic conditions, nutrition,

polypharmacy, and the presence or absence of geriatric syndromes. Aging is further associated with important pharmacologic changes that involve pharmacokinetics, pharmacodynamics, and the toxicity profile of the drugs. These changes increase the risk of therapeutic complications partly because of the different behavior of the disease in an older patient population and partly because of a decreased tolerance to treatment in some older patients (Balducci & Yates, 2010)

2.2.2 Gender

When addressing the difference between CKD in men and women, it must be noted that eGFR is based on a patient's sex, among other variables. The two most common equations for assessing eGFR, the MDRD (Modification of Diet in Renal Disease) and CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) equations, both use sex as a variable. They are based on the assumption that for a given creatinine level, men will have higher levels of kidney function than women due to higher muscle mass and increased creatinine generation among men (Pounds, 2013). Though the prevalence of chronic renal failure may be higher in women, the incidence of ESRD seems to be higher in men, indicating that the progression rate of renal disease may be faster in men than women. Based on the most recent *US Renal Data System (USRDS) annual data report*, the prevalence of chronic renal failure between the years 2007 and 2012 was higher in women (15.1%) than in men (12.1%). Women had a higher prevalence of high urinary albumin to creatinine ratio (9.6% versus 8.1% in men) and a higher prevalence of decreased GFR (7.6% versus 5.4% in men). Nonetheless, the incidence of ESRD appears to be higher in men than women. Based on the most recent US Renal Data System data, 57.8% of the patients with a new onset ESRD were men. Furthermore, 56.3% of the prevalent dialysis patients were males, as were 59.7% of the kidney transplant recipients in the USA. Several other studies found similar results.

Many possible mechanisms for the protective effect of female gender on CKD patients have been suggested. These include gender differences in kidney anatomy, kidney hemodynamic stress response, effect of sex hormones, diet, lipid metabolism, and blood

pressure. Anatomically, the kidney is usually larger in men, due to a larger body surface area. Some studies have shown a smaller number of glomeruli in female kidneys (Neugarten & Golestaneh, (2013). The hemodynamic stress response of the kidney differs between men and women; men may develop higher filtration fraction in response to angiotensin II infusion. During hyperglycemia, women exhibited a reduction in renal blood flow and an increase in renal vascular resistance and filtration fraction, whereas males exhibited no significant renal hemodynamic changes (Khunti et al, 2021) These findings may explain the lack of renal protection among diabetic women. Lifestyle differences between men and women has been suggested as another possible explanation for the influence of gender on CKD. A high protein and high caloric dietary intake, which characterizes men more than women, is associated with the development and the progression of kidney disease. High levels of LDL, triglycerides, and uric acid, and low levels of HDL are associated with accelerated kidney disease progression. These trends are more common in men, and are influenced by nutrition and lifestyle. The role of sex hormones in the pathogenesis of renal injury has gained a lot of attention. Several animal studies demonstrate a harmful influence of testosterone and protective influence of oestrogen on processes involved in kidney injury (Ricardo et al, 2019). Testosterone induces podocyte apoptosis (playing an important role in the development of glomerulosclerosis) and TGF-β1 expression which is connected to tissue fibrosis while estradiol inhibits these processes. It was demonstrated that testosterone induces proximal tubular cell apoptosis in human cells in vitro (Verzola et al, 2019) In addition, estradiol has a direct influence on mesangial cells, decreasing extracellular matrix production and glomerulosclerosis. Nitric oxide (NO) synthase activity is also influenced by sex hormones. For example, estrogen depletion has been associated with a decrease in the level of NO synthesis (endothelial and inducible NO synthase) in the kidney medulla (Maric, Xu, Sandberg & Hinojosa-Laborde, 2015). Another study found an age-dependent reduction in NO synthase activity in the kidney cortex of male rats, but not in female rats. Generally, NO synthase inhibition is associated with renal injury. Recent animal studies have shown a protective role of NO in acute kidney injury. Additional influences of sex hormones on key factors in kidney injury have been noted: the renin–angiotensin system

is induced by testosterone and inhibited by estrogen; estradiol inhibits the synthesis of endothelin, as well as its vasoconstrictor and inflammatory effects; estrogen also plays a role in decreasing kidney oxidative stress by suppressing NADPH oxidase activity (Ji et al, 2017).

2.3 Clinical Characteristics of Cancer and Renal Insufficiency

The clinical status of cancer patients varies. This is majorly depending on the stage of cancer and presence of other co- morbidities. TNM is the most widely used cancer staging system as recommended by American Joint Committee on Cancer and Union for International Cancer control. T stands for primary tumor. TX means that there is no information about the tumor or it cannot be measured. T0 means that there is no evidence of a tumor. Tis refer to a tumor "in situ." This means that the tumor is only found in the cells where it started. It has not spread to any surrounding tissue. T1-T4 describe the size and location of the tumor, on a scale of 1 to 4. A larger tumor or a tumor that has grown deeper into nearby tissue will get a higher number. N for lymph nodes spread. It indicates whether tumor has spread to the lymph nodes, in which group of lymph node and how many. N0- there are no lymph nodes involvement. N1-3 indicates number and location of lymph nodes that contain cancer depending on how far it has spread. M stands for distance metastasis to other body organ. M0 there is no spread to distant site and M1 there is metastasis to distant organ. Physical exams, imaging scans and laboratory test are used to determine clinical cancer stage. Pathological staging can be done through surgery and biopsy. Beside staging, cancer grading can also be done depending on whether metaplastic cells resemble original cell or not. There are generally 3 grades of cancer: Grade 1 – the cancer cells look very similar to normal cells and are growing slowly (low grade). Grade 2 – the cells don't look like normal cells and are growing more quickly than normal (intermediate grade). Grade 3 – the cancer cells look very abnormal and are growing quickly (high grade). GX cancer grade cannot be determined (AJCC\UICC, 2022).

Cancer staging and grading are used to predict the clinical behavior of malignancies, establish appropriate therapies, and facilitate exchange of precise information between

clinicians. The effect of cancer on the kidney is multifaceted. Renal cell carcinoma, adrenal gland cancers and cancers in the nearby tissue can lead to direct invasion and destruction of kidney tissue. Metastasis and obstructive uropathy and hydronephrosis is common in stage 4 disease. Chronic kidney disease in patients with advanced cancer is frequently associated with malignant ureteral obstruction leading to obstructive nephropathy. Neoplastic ureteral infiltrations associated with large tumor masses cause kidney injuries and reduce the glomerular filtration rate (GFR). Acute renal failure in advanced tumor is a serious complication of cancer and constitutes a major source of morbidity and mortality. Current data suggest that ARF has the potential to substantially jeopardize the chances of cancer patients receiving optimal treatment and a potential cure. The pathways leading to ARF in cancer patients are common to the development of ARF in other conditions. However, ARF may also develop due to aetiologies arising from cancer treatment or the disease itself, including: nephrotoxic chemotherapy agents, post-renal obstruction, compression and infiltration by malignancy, tumour lysis syndrome, uric acid, sepsis and contrast agent nephropathy (Lameire et al 2015). Tumor lysis syndrome (TLS) is a serious, sometimes life-threatening oncologic emergency in metastasized cancers. It is caused by rapid and massive cellular lysis and subsequent release of tumor cell contents and cytokines into the bloodstream. Clinical consequences of TLS include nausea, vomiting, cardiac dysrhythmias and acute kidney injury resulting from hyperuricemia, hyperphosphatemia, or hyperkalemia, and seizures or other symptoms of hypocalcemia. Patients with advanced cancer (stage 3 or 4) have a higher risk for kidney failure requiring replacement therapy (KFRT), and that risk differs by cancer type. Study done by Kim, Kim & Suh (2021) at National University Medical School, Korea, and colleagues reported in the *American Journal of Kidney Diseases*, using the Korean National Health Insurance Service database, examined KFRT risk among 824,365 Korean patients with cancer compared with 1,648,730 patients without cancer matched by age, sex, estimated glomerular filtration rate (eGFR), diabetes status, and hypertension status. KFRT was required for 1.07 patients with cancer compared with 0.51 patients without cancer per 1000 person-years. Advanced cancer was significantly associated with a 2.3-fold increased risk for KFRT, in a fully adjusted model. Among

patients with chronic kidney disease (CKD), those with cancer and those without cancer had a significant 1.4-fold increased risk for KFRT. Among patients with proteinuria, cancer was associated with a significant 1.3-fold increased risk for KFRT. In conclusion there are enough evidence that advanced stage 3 and 4 cancers increase risk of renal insufficiency of which the end result can be end stage kidney failure needing renal replacement therapy (KFRT).

2.4 Cancer Treatment Modalities and Renal Insufficiency

2.4.1 Chemotherapeutic Anti- Cancer Agents

Most of the chemotherapeutic agents in clinical practice may have detrimental effect on the kidney. Various renal injury mechanisms are involved. Drugs can cause renal injury by inducing a varying combination of intra-renal vasoconstriction, direct tubular toxicity and intra-tubular obstruction as a result of various products of tumor lysis syndrome. In addition, the kidneys are an important site for xenobiotic metabolism and may transform relatively harmless parent compounds into toxic metabolites. High metabolic rate and the workload of renal cells results in increased sensitivity to toxicants and a high sensitivity to vasoactive agents (Cummings & Schnellmann, 2013). Because the kidneys are a major elimination pathway for many antineoplastic drugs and their metabolites, renal impairment can result in delayed drug excretion and metabolism of chemotherapeutic agents, resulting in increased systemic toxicity. Many drugs require thus dose adjustment when administered in the setting of renal insufficiency (Perazella, 2012). Same study by Perazella (2012), revealed that another important risk factor is the patient's underlying genetic makeup, which is likely to explain heterogeneous response to chemotherapeutic agents. Gene polymorphisms in the cytochrome P450 enzyme system, which favor reduced metabolism and renal excretion, may enhance nephrotoxic risk. There is also presence of an unrecognized abnormal GFR, higher rates of renal oxidative stress and excessive levels of angiotensin-II/endothelin, all of which increase drug nephrotoxicity mostly in elderly individuals (Jerkić, Vojvodić & López-Novoa, 2011).

In a study of 4684 adults (mean age 58 years) undergoing treatment for cancer in 15 French centers [the Renal Insufficiency and Anticancer Medications (IRMA) study] found that 50–60% had biochemical evidence of impaired glomerular function (Launay-Vacher, 2010). Of the patients who were treated with an anti-cancer drug, 79.9% received at least one drug that required a dosage adjustment or for which there were no data for use in patients with renal insufficiency and 80.1% received at least one drug that was potentially nephrotoxic. The Belgian Renal Insufficiency and Anticancer Medications (BIRMA) study including 1137 cancer patients with solid tumors and in whom an SCr was available found a prevalence of an elevated SCr ≥ 1.2 mg % (≥106 μmol/L) of 14.9%, but 64.0% had an eGFR ≤ 90 mL min/per 1.73 m^2 (Janus et al., 2010). But on classifying only patients with an eGFR < 60 mL/min as having CKD, the prevalence of 'true' CKD in the BIRMA study is thus 196 on a total of 1137 patients (17.2%). In all, 78.6% of treated patients (n = 1087) were receiving at least one drug that needed dosage adjustment and 78.1% received at least one potentially nephrotoxic drug. In several of these patients the dose was not appropriately adjusted in accordance to the decreased renal function. Study done by (Li, Liu &Virnig, 2017) involving 28,048 women diagnosed with breast cancer found that 6-month cumulative incidence of AKI was 0.80% for chemotherapy-treated patients, compared with 0.30% for untreated patients (P < 0.001). The findings showed that adjuvant chemotherapy was associated with increased risk of AKI in women diagnosed with early-stage breast cancer. The risk seemed to vary by regimen type, but the differences were not statistically significant

2.4.2 Radiation Therapy

Radiation therapy is a known treatment modality for most of the patients with various types of cancers with or without surgery. Main types of radiation therapy are external beam or internal beam radiation. This is utilized to treat cancer especially during instances where a patient is not able to undergo surgery. Radiation therapy remains an important component of cancer treatment with approximately 50% of all cancer patients receiving radiation therapy during their course of illness; it contributes towards 40% of curative treatment for cancer (Baskar, Lee, Yeo & Yeoh, 2019). In external beam radiation,

radiation from a source is directed onto the part of the body containing the tumor. In internal beam radiation (brachytherapy) the source of radiation which can be an implant or drug are used to directly deliver radiation to affected part of the body. The highly multiplying cancerous cells are more sensitive to radiation than normal cells- leading to their DNA destruction and cells death arresting growth of tumor and shrinkage. However, radiotherapy treatment also affects normal body cells leading to various side effects like nausea and vomiting, blurry vision, alopecia, skin changes, fatigue, headache, hearing loss (Baskar et al, 2019). Additionally, Radiation nephropathy can occur as result of kidney injury and impairment of kidney functions as result of ionizing radiation. Cancer cells turnover and destruction is high during radiotherapy. High levels of both uric acid and phosphate released render patients with the tumor lysis syndrome particularly high risk for crystal-associated acute kidney injury, because uric acid precipitates readily in the presence of calcium phosphate, and calcium phosphate precipitates readily in the presence of uric acid (Park et al, 2021).

2.4.3 Surgery

Surgical management is treatment of choice for early stage cancers. There are various reasons why surgery is done on a patient. Surgery can be done to take biopsy for diagnosis and staging of cancer. Most important of all localized early stage cancer can be excised and resected. Less invasive procedures like laparoscopic or robotic surgery can be done. Surgery alone can lead to cure in localized non metastasized disease. Debulking to reduce size of tumor can be done. Palliative surgery is done to relieve pressure and pain, stop blockage and bleeding. Reconstructive surgery to restore appearance and function of body organ (Saito et al, 2021). Surgery involving any part of the urinary system may directly interfere with functionality of the system. Surgery for the primary or secondary cancers in the kidney tissue can lead to the destruction of nephrons and tubular system during total or partial nephrectomy leading to renal failure. Age and glomerular filtration rate loss related to renal cancer surgery, whether due to partial or radical nephrectomy, influences the risk of chronic kidney disease and is a good predictor of overall survival in cancer patient (Zabell et al, 2017). According to the findings of a population-based study

presented at the 2022 European Association of Urology congress, patients who undergo surgical treatment of renal cell carcinoma (RCC) are at increased risk for end-stage kidney disease (ESKD). Development of ESKD in these patients increases their risk for death. Like- wise ureteral stent put in place to relieve urine blockage can become encrusted and predispose an individual to kidney stones, urinary tract infection and pyelonephritis increasing chance of renal dysfunction. Nephrostomy tube can also get blocked leading to hydronephrosis and renal failure. Damage to renal tubules can also occur as result of catabolic stress response and profound hemodynamic deterioration during surgery. Hyper catabolic state accompanying surgery may worsen electrolyte imbalance and cause tumor lysis syndrome affecting renal function (Park et al, 2021) A Study by Saito et al (2021): Japanese Joint Committee of Lung Cancer Registry- preoperative renal dysfunction and long-term survival after surgery for non-small cell lung cancer found that Preoperative renal dysfunction may be adversely associated with overall survival after lung cancer surgery. This finding therefore, could aid patients to set proper expectation of the risks and benefits about surgery for lung cancer. Study by Sahin, Bilir & Ayaz, 2014) reported of a case in which a patient with short bowel syndrome after colonectomy presented with prerenal acute renal failure even though he had sufficient oral intake and nutrition possibly due to water and electrolyte depletion due to limited absorptive capacity.

2.4.4 Immunotherapy

Immunotherapy is a type of cancer treatment that uses substances made by the body or in a laboratory to boost the immune system and help the body find and destroy cancer cells. It can be used alone or in combination with chemotherapy and/or other cancer treatments options. The different types of immunotherapy include: Monoclonal antibodies and immune checkpoint inhibitors, Non-specific immunotherapies, Oncolytic virus therapy, T-cell therapy and Cancer vaccines. Study by Alain and others on 16 patients suffering from metastatic renal cell carcinoma found that ARF occurred frequently during IL-2 therapy. The decrease in renal function begins immediately after the initiation of therapy and the magnitude of worsening is contemporary with the end of cytokine infusion. A rapid return to control values is noted following discontinuation of treatment. Large scale

study done in France between 2015- 2017 by Izzedine & Perazella (2017) found biopsy-proven (PD-1 inhibitor monoclonal antibody) pembrolizumab- related nephropathies. Kidney involvement related to pembrolizumab can lead to acute kidney injury and/or nephrotic syndrome associated with acute interstitial nephritis. For patients who developed renal injury, pembrolizumab withdrawal coupled with corticosteroid therapy was most effective treatment for kidney function recovery. Checkpoint inhibitors (CPIs) have drastically improved metastatic cancer outcomes. However, immunotherapy is associated with multiple toxicities, including acute kidney injury (AKI). A single AKI episode was identified as an independent risk factor for mortality in these patients and age and baseline renal function were risk factors for the development of AKI (Garcia et al, 2022). Acute interstitial nephritis is most common cause of acute kidney injury associated with immune checkpoint inhibitors caused by over activation of immune system due to cytotoxic T lymphocyte associated antigen 4 and programmed cell death receptor 1/ programmed cell death ligand 1 inhibition. Kidney injury in patient on immunotherapy treatment for cancer is common. Serial and close monitoring of renal function is necessary for early intervention and management (Izzedine & Perazella, 2017).

2.4.5 Hormonal Treatment of Cancers

Hormone therapy is administration of sex hormone to treat cancers that use hormones to grow. Hormonal therapy also can involve surgery to remove hormone-making organs like testis and ovary. Such cancers include breast and prostate cancers. This type of cancer treatment helps in slowing or stopping growth of cancers that uses hormone to grow. It is also called endocrine treatment of cancers. Hormone therapy is most often used along with other cancer treatments. It can be used as neoadjuvant to shrink tumor before main treatment of surgery. It can also be given as adjuvant therapy after surgery to arrest growth of remaining cancerous cells after surgery reducing chance of recurrence. Population based cohort study in Scotland between 2012- 2017 in prostate cancer containing 10,751 patients followed for 41,997 person years (10751 person followed up for 1 year = 10751person year), during which there were 618 hospitalizations with acute kidney injury. Prostate cancer patients had higher rates of acute kidney injury compared with cancer-free

controls (adjusted Hazard ratio = 1.47 95% Confidence interval 1.29, 1.69). However, prostate cancer patients currently using hormone therapy (adjusted HR = 1.14 95% CI 0.92, 1.41), including gonadotropin-releasing hormone (GnRH) agonists (adjusted HR = 1.13 95% CI 0.90, 1.40), had slight increase in acute kidney injury compared with prostate cancer patients not using hormone therapy after adjusting for potential confounders. The conclusion from that study was that there was little evidence that gonadotropin-releasing hormone agonists were associated with marked increases in acute kidney injury. Androgen deprivation therapy (ADT) remains widely used in the treatment of prostate cancer at various time points in the disease course. A potential risk of ADT that has been investigated more recently is acute kidney injury (AKI) requiring hospitalization. The first of these studies by (Daskivich, 2021) analyzed 10,250 men with newly diagnosed non metastatic prostate cancer from 1997 to 2008 in the UK Clinical Practice Research Datalink. This study concluded that use of any ADT (Odd ratio 2.48, 95% CI 1.61–3.82)—in particular combined androgen blockade with gonadotropin-releasing hormone (GnRH) agonists and oral antiandrogens (OR 4.50 [95% CI, 2.61–7.78]) and GnRH agonists alone (OR 1.93 [95% CI, 1.20–3.10])—was associated with higher risk of AKI compared with no ADT. Similar study done by (Lapi et al, 2013) found that use of androgen deprivation therapy (ADT) in the treatment of advanced prostate cancer has been shown to delay the clinical progression of the disease. However, the testosterone suppression associated with this therapy may lead to a hypogonadal condition that can have detrimental effects on renal function. Surgical castration with bilateral orchiectomy was not found to be associated with AKI. There are several plausible mechanisms for why ADT may cause AKI: (1) ADT-induced hyperglycemia and dyslipidemia may affect renal glomerular function by changing the morphology of the interstitial tubular membrane, (2) ADT may blunt the vasodilation of renal vessels mediated by testosterone via nitric oxide, leading to ischemic injury, and (3) ADT-induced hypogonadism reduces estrogen, which is thought to be protective against renal ischemic injury.

2.5 Cancer and Renal Insufficiency

2.5.1 Cancer Types and Renal Insufficiency

Cancer is the second leading cause of death worldwide, accounting for nearly 10 million deaths in 2020, or nearly one in six deaths. Of these 10 million 70% were in low-and-middle-income countries (WHO, 2020). Globally most common cancers are lung, colon and rectum, breast, stomach and prostate cancers. Prevalence of cancers in sub- Sahara is staggering. 801 392 new cancer cases and 520 158 cancer deaths were estimated to have occurred in sub-Saharan Africa in 2020. Cancer is the third leading cause of death in Kenya and second leading cause of NCD deaths after cardiovascular diseases accounting for 7% of overall mortality in the country (MoH, Kenya, 2020). Most cancers are known to be associated with reduction in renal function as complication leading to increase morbidity and mortality in patients suffering from cancers (Janus et al, 2010). As different tumor types can behave differently, and are treated with different treatment modalities, it is necessary to look at renal function in different tumor types on different treatment modalities.

Study done in Turkey (Dogan et al, 2015) showed that at least 27.1% of cancer patients are suffering from renal insufficiency and need some chemotherapeutic drugs adjustment. Another study found that overall prevalence of renal dysfunction ranges from 12 to 25% across many cancer patients (Kitchlu et al., 2019). These results clearly demonstrate that, when patients with cancer develop acute or chronic kidney disease, outcomes are inferior, and the promise of curative therapeutic regimens is lessened as demonstrated by Dogan et al. (2015).

Table 2.1: Possible Causes of Renal Insufficiency in Cancer Patients

Pre- renal	Intrinsic	Post renal
Fluid depletion- poor intake, diarrhea, vomiting, hypercalcemia	**Glomerular**- membranous nephropathy, amyloidosis, pamidronate associated collapsing nephropathy, light chain deposition disease **Tubulointerstitial**- Acute tubular necrosis, lymphomatous infiltration of kidney, light chain deposition disease, drugs e.g. cisplatin, ifosfamide, IV contrast, casts nephropathy **Vascular-** Thrombotic thrombocytopenic purpura and Hemolytic uremic syndrome (post hematopoietic transplant, mitomycin c, gemcitabine), tumor infiltration	**Intra- tubular obstruction-** uric acid nephropathy, cast nephropathy, methotrexate **Extra renal obstruction-** bladder outlet obstruction, ureteral obstruction(primary disease, retroperitoneal lymphadenopathy, retroperitoneal fibrosis)

2.5.2 Breast Cancer

Breast cancer is the most common cancer in women accounting for 30% of all newly diagnosed cancers (Siegel, Miller & Jemal, 2020). Cancer metastasis to different parts of the body. Direct invasion of kidney and urinary system pathway has direct consequence on renal function.

Toxins from cancer cell break down especially in patient on treatment may result in tumor lysis syndrome that can cause kidney injury. Renal failure is an important factor limiting the treatment of breast cancer patients as patients with impaired renal function often experience reduced renal excretion or metabolism and changes in absorption and drug distribution, which may lead to increased treatment-related toxicity (US Food and Drug Administration, 2014). In hemodialysis patients, it is difficult to determine the safe and effective dosage and dosing schedule of anticancer drugs, as well as the best time for hemodialysis, which makes it difficult to develop an appropriate treatment regimen. Currently, apart from the case report by Modi, Madabhavi, Patel & Anand (2018), there are few studies on the treatment of breast cancer in patients with end-stage renal disease,

and these patients rarely successfully complete a series of standard regimens of neoadjuvant therapy and surgery.

2.5.3 Colorectal Cancer

Cancer can spread by directly growing into and invading nearby abdominal and pelvic organ from primary tissue of rectum or colon because of the proximity of the organ. Metastasis can also happen through blood streams and lymphatic system to other organs like liver, lungs, brain and bones. Secondary deposits grow within renal tissue destroying renal parenchyma. It can also spread to lower urinary system like ureter and bladder causing obstruction. Nephrotoxic chemotherapy agents, radiotherapy, infiltration by malignancy, tumor lysis syndrome, uric acid, sepsis and contrast agent nephropathy are possible cause of renal insufficiency. Post- operative acute renal failure is major factor of morbidity and mortality in patient with colorectal malignancy (Hossein et al, 2015). The retrospective cohort study by Ren, Zhu, Li & Xia (2025) found that colorectal cancer (CRC) patients commonly exhibited decreased kidney filtration function. Lower estimated glomerular filtration rate (eGFR) was associated with significantly worse clinical outcomes: patients with lower eGFR had higher rates of disease recurrence and poorer overall prognosis compared with those with higher eGFR, even after adjusting for tumor stage and clinical variables. This suggests that impaired renal function is an independent predictor of CRC recurrence and prognosis, highlighting the potential utility of eGFR as a prognostic biomarker in clinical practice. Additionally, in patients with metastatic colorectal cancer receiving trifluridine/tipiracil therapy, pre-existing renal impairment was significantly associated with an increased risk of early severe neutropenia, a serious hematologic adverse event. While the study did not primarily focus on cancer progression, it demonstrated that renal insufficiency can significantly affect treatment tolerability and safety in CRC patients, suggesting clinicians should carefully monitor kidney function before and during chemotherapy to mitigate adverse outcomes (Saito el al, 2024)

2.5.4 Prostate Cancer

Because of the close proximity prostate cancer can directly invade urethra and urinary bladder causing blockage and hydronephrosis although metastasis directly to the kidney tissue is rare findings of which about 50 case reports has been described so far (Munshi et al, 2019). Urine stasis and frequent urinary tract infection as result of blockage can also cause pyelonephritis with subsequent sepsis which can affect kidney functions., hence causing renal insufficiency. There are also reports of hormone-resistant, ureteric metastatic type of prostate cancers (Tsutsumi et al, 2017). The multicenter analysis of 222 patients with prostate cancer from the French Renal Insufficiency and Anticancer Medications (IRMA) cohort found that while only 14.9% had elevated serum creatinine (>110 μmol/L), the prevalence of renal insufficiency estimated by kidney function formulas was much higher — 62.6% using Cockcroft-Gault and 55.9% using aMDRD — indicating subclinical RI missed if relying on creatinine alone. A majority of patients were on anticancer drugs requiring dose adjustments due to RI (Launay-Vacher,2019)

2.5.5 Esophageal Cancer

A variety of kidney complications can occur among patients with cancer including acute kidney injury, chronic kidney disease, proteinuria and nephrotic syndrome, and electrolyte disorders. Patients with cancer may present with proteinuria and nephrotic syndrome, which can be caused by the underlying malignancy (paraneoplastic) or its treatment (Shaheen, Ghibour & Alsaid, 2017). The most common paraneoplastic glomerular diseases are membranous nephropathy (MN) and minimal change disease (MCD). Chemotherapy-associated glomerular diseases may present at various times during treatment, and therefore, patients receiving these drugs should be monitored for the development of proteinuria and/or kidney function impairment (Murphy et al, 2018). Electrolyte disorders are commonly seen in patients with malignancies, and in many cases, the etiologies of these disorders are the same as those seen in the general population. In other circumstances, electrolyte disorders can be caused by cancer (ie, paraneoplastic syndromes) or its treatment (Murphy et al, 2018). Common abnormalities

include hyponatremia, hypernatremia, hypercalcemia, hypokalemia, hyperkalemia, hypophosphatemia, hyperphosphatemia, and hypomagnesemia. The most common pattern of oesophagal cancer metastases (ECM) is to the lymph nodes, lungs, liver, bones, adrenal glands, and brain. On the other hand, unexpected metastasis (UM) spread to uncommon sites has increasingly been reported and consequently affected the pathway of diagnosis, staging, and management. Between 1982 and February 2017 using the PubMed database (*US National Library of Medicine, Bethesda, Maryland*), a systematic medical literature search of 10049 articles was conducted by the researchers to identify the articles describing uncommon Esophageal cancer metastasis. 164 articles found to be on uncommon esophageal cancer metastasis. The commonest site was said to be renal, pancreas and spleen in the abdominal pelvic cavity (Shaheen, Ghibour & Alsaid, 2017).

2.5.6 Cervical Cancer

When cervical cancer spreads to other areas of the pelvis, it can block one or both ureters leading to hydronephrosis. In hydronephrosis, blocked ureters cause urine to build up in the kidneys causing renal failure if not addressed. Hydronephrosis can be treated using ureteral stent placement. It may also be treated by drainage using a nephrostomy tube that is inserted through the skin and into the affected kidney. Nephrostomy tube is connected onto a bag on the skin to collect urine directly from the kidney. This can be used as an alternative when stents cannot be placed.

2.6 The Conceptual Framework

Renal insufficiency in cancer patients may be caused by a combination of factors. Various types of cancers are known to affect renal insufficiency in various ways. Local invasion of urinary system and distance metastasis are good example. Metabolic derangement and catabolism can generally affect general physiological body functions. Different chemotherapeutic cancer agents may be nephrotoxic to kidney necessitating close monitoring of renal function and good hydration. Tumor degradation products may lead to tumor lysis syndrome leading to uremia and oliguric renal failure due to tubule

precipitation of uric acid, calcium phosphate or hypoxanthine. Different chemotherapeutic agents would be studied and compared in their propensity and association with renal insufficiency. Surgical intervention may also lead to additional metabolic stress and muscle breakdown whose products like myoglobin are nephrotoxic when excreted in renal system. Injury can also occur in surgery involving kidney and urinary pathway down to the urethral orifice. Radiation exposure during radiotherapy may have harmful effect on other body cells beside cancerous one. On the kidney radiation induced kidney injury, specifically radiation nephropathy can result. Cancer immunotherapy is also has been associated with chronic or acute kidney injury, glomerular disease and electrolyte imbalance. Clinical stage of cancer at diagnosis is very important. Stage one cancers are localized and have minimal effect on the body function. Surgical intervention normally can lead to cure. In contrast stage 4 disease has metastasized to the distant organs. The pathological effects on various organs including kidney can result. For metastasized cancers, other treatment options are normally considered. Beginning in the third decade there is physiological loss of kidney function at rate of 1ml/min/m2 per year. The physiological nephron loss and increased likelihood of one suffering from co- morbidity that may affect kidney function, increased chance of older patient diagnosed with cancer, suffer from renal insufficiency. Though female patient suffering from renal insufficiency are known to be more than their male counterparts, men outnumber female in developing end stage renal disease. Investigators have found that estrogen has protective role in the progression of kidney function. The conceptual framework illustrates various causes or risk factors to renal insufficiency which form the independent variables while the dependent variable is the renal insufficiency as shown in figure below.

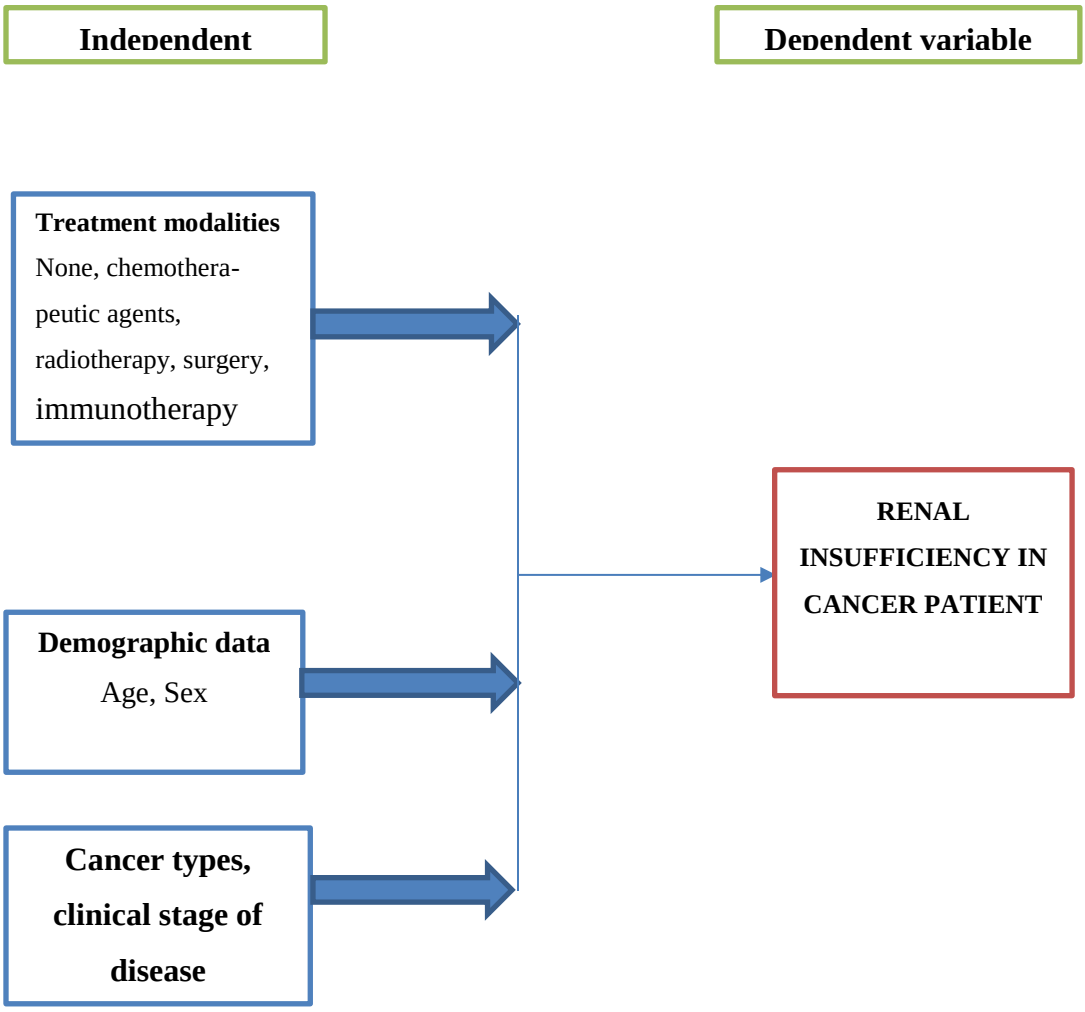

Figure 2.1: Conceptual Framework on Prevalence of Renal Insufficiency in Cancer Patients and Associated Demographic, Clinical and Treatment Factors

CHAPTER THREE

METHODOLOGY

3.1 Introduction

This section presents a description of the research methods. Included in this chapter is the study area, research design, study population, sample size and sampling procedures, data collection tools, pilot study, data collection, measurement of variables, data analysis plan, ethical considerations to be followed and expected outcomes.

3.2 Study Area

This study was conducted at Kenyatta National Hospital (KNH), the oldest and largest referral hospital in the country and East Africa. The hospital is located in the area adjacent to Upper Hill, about two miles west of the Central Business District in Nairobi City. 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. Annually, it serves almost one million inpatients and over 800,000 outpatients. The hospital includes more than fifty wards and twenty-four specialized clinics. Additionally, KNH has twenty-six operating theatres for various surgical procedures and eighty-four intensive care unit (ICU) beds for critically ill patients. 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.

3.3 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.

3.4 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 KNH over a period of 3 months (July–September 2024) and who met the eligibility criteria. 5 major cancers were considered for the study as mentioned below. We limited the analysis to the five major cancers because they represent the largest proportion of our patient population and provide adequate sample sizes for meaningful statistical analysis. Including many rare cancers would have resulted in small, heterogeneous subgroups with limited clinical relevance. Focusing on the most common cancers ensures more reliable, interpretable, and clinically applicable findings regarding renal insufficiency.

3.4.1 Inclusion Criteria

All patients admitted in the Oncological wards or attending outpatient oncology clinics aged 18 years and above, and managed for 5 commonest cancers: breast, prostate, colorectal, esophagus and cervical who gave consent were included in the study.

3.4.2 Exclusion Criteria

The following patients were excluded from the study:

1. Patient with kidney disease secondary to any other cause as identified by nephrologist (Diabetic, hypertensive, Polycystic, HIV related,
2. glomerulonephritis related kidney diseases).
3. Critically or mentally ill patients who are not able to give consent.
4. Patients whose urea, electrolyte and creatinine levels were not available for any reason.

3.5 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 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)

$$n = \frac{1.962 * 0.271\,(1-0.271)}{0.05 \times 0.05} = 304$$

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

$$n + 10\% = \frac{10\ x\ 304}{100} = 31$$

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

3.6 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. Samples were assigned proportionately to both wards and out patients clinics at 10% and 90% respectively. Participants were recruited using stratified proportional consecutive sampling. The study population was stratified by cancer type (esophageal, colorectal,

prostate, breast, and cervical) and by care setting (inpatient wards and outpatient oncology clinics). Sample size allocation across cancer types was proportional to the average caseload at Kenyatta National Hospital. Within each stratum, eligible patients were recruited consecutively until the required sample size was attained, with 10% recruited from inpatient wards and 90% from outpatient clinics. Recording of the in- patients and out -patient numbers were done to make sure that there is no repetition of the same patient over the data collection period. 70 participants were recruited for prostate and cervical cancer, 65 participants for both breast and esophageal cancer and lastly 60 patients for colorectal cancer. This was carried out for a period of 3 months (July- September) until 335 participants were recruited.

3.7 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, histological type of disease and treatment modalities were obtained from patient's files.

3.8 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 oncology outpatient clinic 2 weeks prior to the study (Newman & Odin, 1972). 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. For example, if the questionnaire was

inappropriate for the population under study, the question items were rephrased to focus on the study population and the subject matter. The questionnaire was then tested in the pilot study and any inadequacies corrected.

Reliability was ascertained by 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. Test-retest reliability determined the extent to which test or question items would measure the same construct or thing; in this case, the prevalence of renal insufficiency in cancer patients. During pre-testing, ease of use of the instrument, clarity and rate of response were assessed. The pretest also helped to ensure that the questionnaire was designed with adequate space for responses. Any necessary adjustments were made on the tool based on the findings.

Data on laboratory investigations, clinical staging and treatment modalities was collected from the patient ward files. Demographic data were collected from the patient through face-to-face interviews. The interviews were conducted by trained research assistants.

Estimations of renal function were made by estimating the glomerular filtration rate (GFR) with CKD-EPI formula. The CKD-EPI equation performed better than the MDRD (Modification of Diet in Renal Disease Study) equation, especially at higher GFR, with less bias and greater accuracy. The CKD-EPI medical calculator in micromole/l is used to calculate the estimated glomerular filtration rate of a patient. CKD- EPI medical calculator uses patients age, gender race and creatinine in micromole/l or mg/dl as variables of input. Renal function is then staged in accordance with the clinical practice guidelines published by the Working Group of the National Kidney Foundation and KDIGO (2012) protocol.

3.9 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.

3.10 Study Procedures

Clearance from JKUAT institutional ethics review committee, KNH-UON institutional scientific and ethics review committee and NACOSTI clearance were prerequisites. Clearance was also obtained from the oncology head of the department. The researcher trained two research assistants who administered questionnaires to individual patients through face-to-face interviews. The research assistants had at least a diploma and also knowledgeable in the field of data collection. Research assistants were trained on the research tools and importance of accurate data collection was emphasized. 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.

3.11 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 classified into five stages using GFR in ml/min/1.73m2 G1 (≥90), G2 (60-89), G3a (45-59), G3b (30-44), G4 (15-29) and G5 (<15, or treated by dialysis/renal transplant). In this study estimated GFR of less than 90 mL/min/1.73 m2 was considered as renal insufficiency.

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 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 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, Gauss, Williams & Hosmer, 2008). Results were presented using p values and odds ratios.

3.12 Data Quality Management

To ensure appropriate data quality management, the principal investigator double checked the questionnaires daily for accuracy, consistency and completeness and provided feedback and correction regarding the collected data daily to the research assistants. Additionally, all documents related to the participants and that were intended to be used in the study remained under the custody of the principal investigator for safe keeping so as to ensure confidentiality and could not be accessed by any unauthorized person. Missing data were rechecked in the patients file since both inpatients and out- patient numbers were already recorded. To overcome recall bias most of the data were gotten from the patient file and standardized questionnaires were used. Proportionate sampling was done for participants in the wards or out patients clinics. Training of data collectors done to minimize observer bias. Most common cause of renal failure: DM, hypertension, glomerulonephritis, polycystic kidney disease and HIV were excluded. 5 patients were found to have missing data at the time of analysis and were excluded. The results were also adjusted for possible confounders.

3.13 Ethical Considerations

Clearance was obtained from JKUAT Scientific and Ethic review committee. In addition, clearance to do the research at KNH was obtained from KNH/UON scientific and ethics review committee and also NACOSTI (***License No: NACOSTI/P/24/36871***). Permission was also sought from the head of 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).

CHAPTER FOUR

RESULTS

4.1 Participant Flow Chart and Demographic Characteristic

The following figure shows participants recruitment flow chart

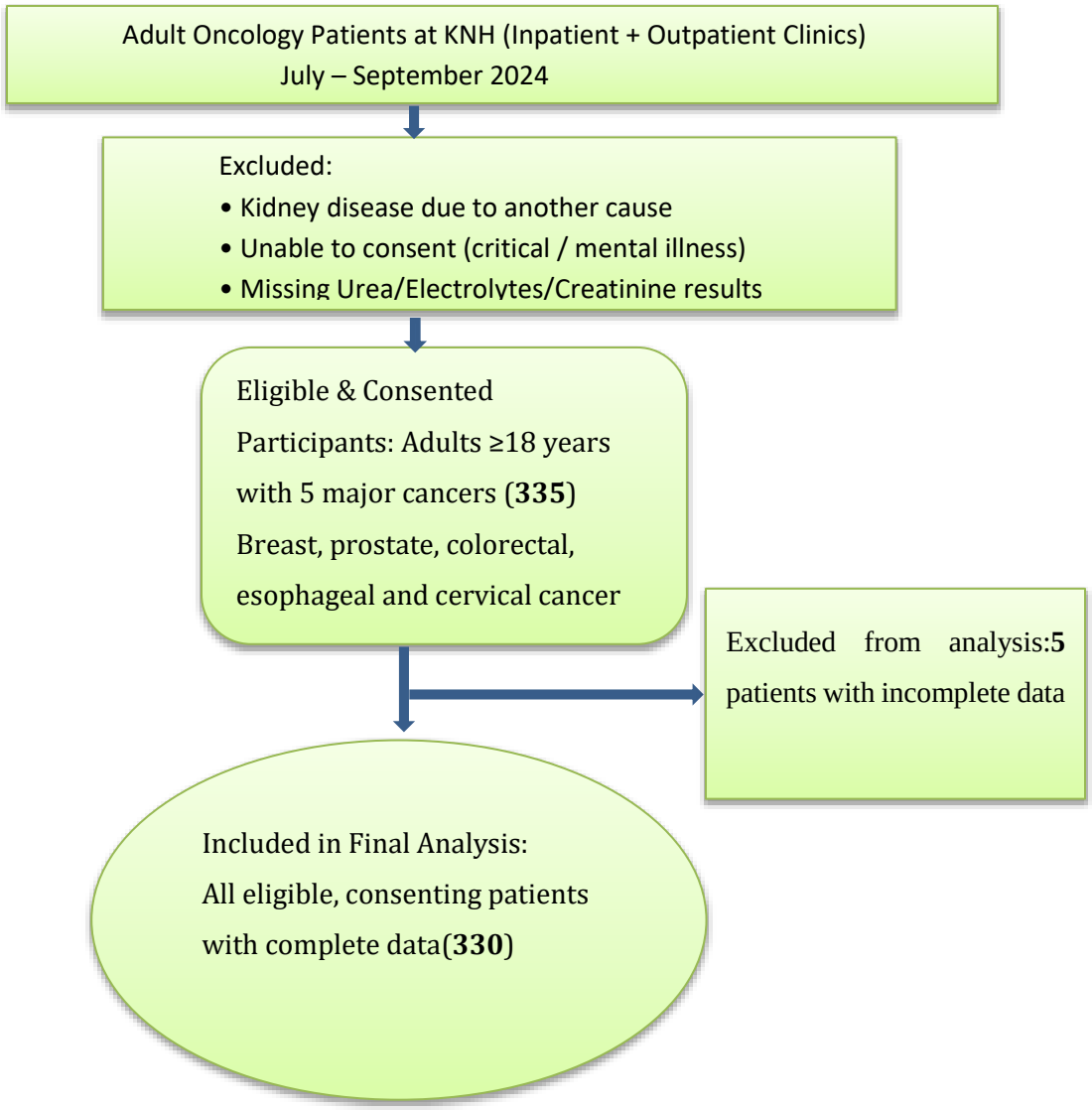

Figure 4.1 Participant Flow Chart

The number of the patients participated in the interview were 335. However, at the time

of data entry 5 patients were found to have incomplete data and were excluded. Therefore 330 patients (98.5% of total participants) were included in data 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 Table 4.1.

Table 4.1: 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

IQR *– Interquartile range*

4.2 Cancer Diagnosis and Clinical Staging

Organ involved

Study involved renal insufficiency among five most common cancers treated at KNH. Cervical and prostate cancers had 70 (21.2%) participants each. Out of the 330 patients, 65 (19.7%) of the patients had breast and oesophageal cancer each while the remaining had colorectal cancer as shown in figure 4.1.

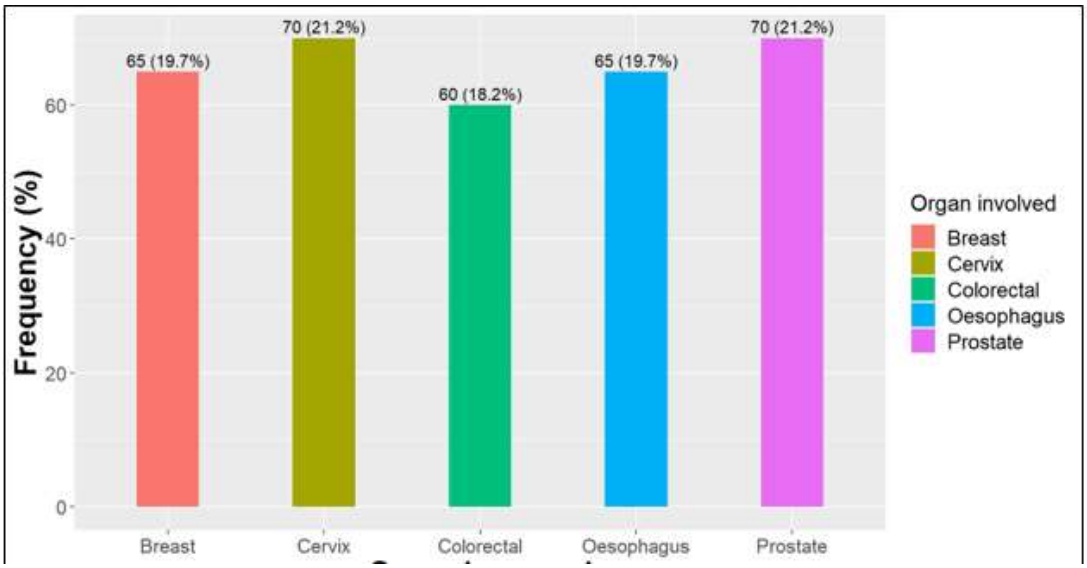

Figure 4.2: Major Cancers in the Study

4.3 Cancer Histopathology Based On Organ Involvement

Of the 65 patients with breast cancer, 64 (98.5%) had ductal cell carcinoma with the remaining one patient having adenocarcinoma. The majority 59 (84.3%) of the patients with cervical cancer had squamous cell carcinoma with 10 (14.3%) having adenocarcinoma and only one patient having a neuroendocrine tumour.

Table 4.2: Cancer Histopathology Based On Organ Involvement

Organ involved	Cancer histopathology	Frequency (%)
Breast (n = 65)	Adenocarcinoma	1
	Ductal cell carcinoma	64 (98.5%)
Cervix (n = 70)	Adenocarcinoma	10 (14.3%)
	Neuroendocrine	1
	Squamous cell carcinoma	59 (84.3%)
Colorectal (n = 60)	Adenocarcinoma	58 (96.7%)
	Neuroendocrine tumour	2
Oesophagus (n = 65)	Adenocarcinoma	10 (15.4%)
	Neuroendocrine tumour	1
	Squamous cell carcinoma	54 (83.1%)
Prostate (n = 70)	Adenocarcinoma	70 (100%)

The colorectal cancers were mainly characterised by adenocarcinoma, 58 (96.7%) while two patients had neuroendocrine tumours. All the patients with prostate cancer had adenocarcinoma (Table 4.2).

4.4 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. The majority, 181 (54.9%) were diagnosed in stage 4 and 105 (31.8%) in stage 3. Thirty-nine (11.8%) of the patients were diagnosed in stage 2 with only five patients diagnosed in stage 1 as shown in figure 4.2.

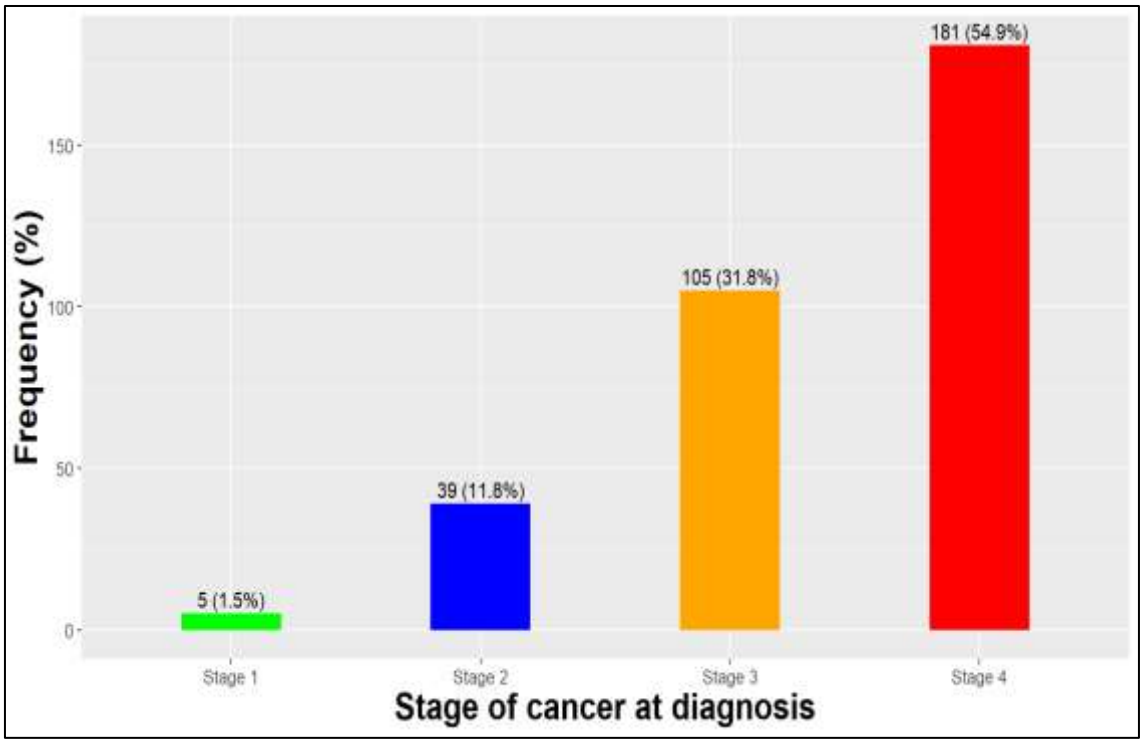

Figure 4.3: Stage of Cancer at Diagnosis

4.5 Stages of Cancer Diagnosis Based on the Organ Involved

The results in table 4.3 show that there was late diagnosis for all the cancers. None of the patients with breast, prostate and oesophageal cancers were diagnosed in stage 1. Of the five patients diagnosed in stage 1, 2 had cervical cancer while three had colorectal cancer. Of the 65 patients with breast cancer, the majority 47 (72.3%) were diagnosed in stage 4 while 11 (16.9%) were diagnosed in stage 3. Seven patients were diagnosed in stage 2. Of the 70 patients with cervical cancer, 32 (45.7%) were diagnosed in stage 3 while 29 (41.4%) were diagnosed in stage 4. The rest were diagnosed in stages 1 and 2. Most of the patients with prostate cancer, 53 (75.7%) were diagnosed in stage 4 as shown in table 4.3.

Table 4.3: Stage of Diagnosis and the Affected Organ

Organ involved	**Stage 1 n (%)**	**Stage.2 n (%)**	**Stage 3 n (%)**	**Stage 4 n (%)**	**Total**
Breast (n = 65)		7(10.7)	11 (16.9)	47 (72.3)	65 (100%)
Cervix (n = 70)	2(2.9)	7(10)	32 (45.7)	29 (41.4)	70 (100%)
Colorectal(n=60)	3(5)	5(8.3)	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 (12.9)	8 (11.4)	53 (75.7)	70 (100%)
Total	5(1.5)	39 (11.8)	105 (31.8)	181 (54.9)	330 (100%)

4.6 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 blood workup like full blood count, liver function test and latest renal function test to start cancer management while the remaining five were waiting for stabilization because they were too weak to start treatment.

In terms of chemotherapy, 130 (39.4%) of the patients were on platinum derivatives, 68 (20.6%) were on taxanes and 52 (15.8%) were on antimetabolites. A total of 16 (4.8%) of the patients were classified as others and they were on one of these medications: etoposide, irinotecan, vincristine, cyclophosphamide and Adriamycin.

Of the 330 patients, 152 (46.1%) underwent surgical operation, 126 (38.2%) were done radiotherapy and 40 (12.1%) received immunotherapy. The patients were also treated with hormonal therapy where 58 (17.6%) got goserelin, 29 (8.8%) got abiraterone and 7 (2.1%) got letrazole/anastrazole. Other hormonal therapies were; fulvestrant, tamoxifen, bicalutamide (casodex) were received by 10 patients (3%). Majority of the patients 261(88.2%) received multiple modes of cancer management and only 35(11.8%) received single modality. Chemotherapy and hormonotherapy were received by majority and other are as shown in table 4.4.

Table 4.4: Cancer Management Modalities

Management modality	**Frequency (%)**
Already on cancer treatment	
Yes	296 (89.7%)
No	34 (10.3%)
Reasons not on cancer treatment (n = 34)	
Not yet finalize blood 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%)
Patients on single or multiple treatment	
Multiple treatment	261(88.2%)
Single treatment	35(11.8%)

Management modality	Frequency (%)
Only surgery	3(8.6%)
Only radiotherapy	2(5.7%)
Only immunotherapy(Nivolumab,Regorafenib)	3(8.6%)
Only hormonal (Goserelin, Abiraterone)	13(37.1%)
Only chemotherapy(Cisplatin,docetaxel)	14(40.0%)

4.7 The Prevalence of Renal Insufficiency among Cancer Patients

Patients with renal insufficiency were defined as those with eGFR using (CKD-EPI) of 89 and below. There were 127 patients with eGFR of less than 90 giving us a prevalence of 38% (95% CI 33%, 44%) (Figure 4.3).

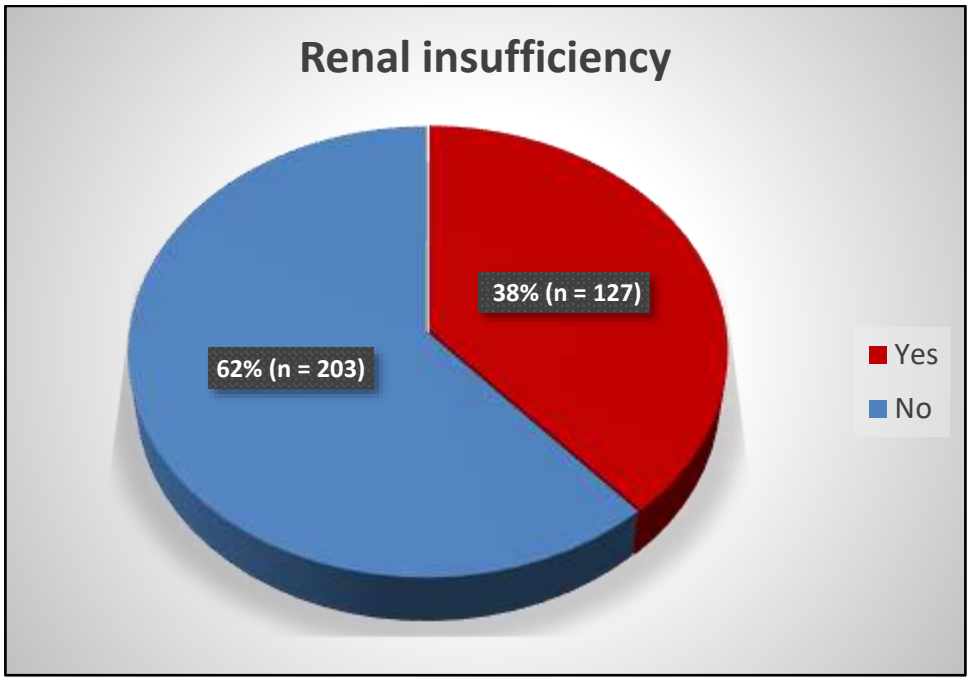

Figure 4.4: Proportion of Patients with Renal Insufficiency

4.8 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%), stage G3b (eGFR 30-44) were 8 (2.4%). The rest is shown n figure 4.4.

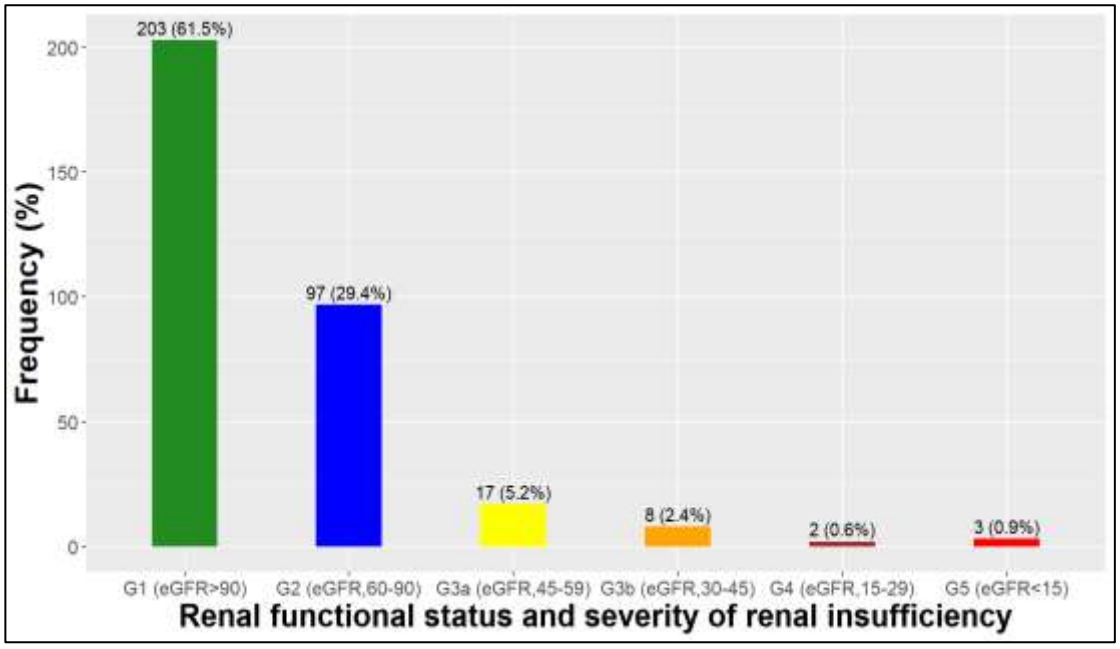

Figure 4.5: Renal Functional Status and Severity of Renal Insufficiency among Cancer Patients

4.9 Factors Associated with Renal Insufficiency among Patients Treated with Cancer

From our 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 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). 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 letrazole had 4.12 times higher odds compared to those who were not on letrazole OR 4.12 (95% CI 0.87, 29.07).

Variables with p values of less than 0.25 were selected for the multivariable model (Bursac et al., 2008). 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 4.5.

Table 4.5: Factors Associated with Renal Insufficiency among Patients Treated for Cancer.

	Renal insufficiency					
Factors	**Yes n = 127**	**No n = 203**	**cOR (95% CI)**	**P-value**	**aOR (95% CI)**	**p-value**
Demographic characteristics						
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		
>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						

	Renal insufficiency					
Factors	**Yes n = 127**	**No n = 203**	**cOR (95% CI)**	**P-value**	**aOR (95% CI)**	**p-value**
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		
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***			

Single and multimodal cancer treatment

	Rena insufficiency			
	Yes	no		
Unimodal	13	22	1.03 (0.50, 2.15)	0.93
Multimodal	99	162	***Reference***	

CHAPTER FIVE

DISCUSSION, CONCLUSION AND RECOMMENDATIONS

5.1 Introduction

Renal insufficiency is highly common in cancer patients and has been linked to lower overall survival rates and higher cancer-related mortality. Consequently, it is essential to screen cancer patients for renal insufficiency using a reliable method to assess kidney function (Launay-Vacher et al., 2016). The Renal Insufficiency and Cancer Medications (IRMA) study found that chronic kidney disease (CKD) is more common among cancer patients compared to the general population and that cancer patients with CKD have lower survival rates than those without kidney disease (Launay-Vacher, 2010).

Acute renal failure (ARF) in cancer patients is a severe complication associated with high rates of illness and death. ARF is characterized by a rapid and sustained reduction in glomerular filtration rate (GFR), occurring within hours to days. Nearly 10% of cancer patients undergoing chemotherapy or targeted therapies may face serious kidney injury requiring hospitalization. Among critically ill cancer patients (CICPs), ARF occurs in 12% to 49% of cases, with 9% to 32% needing renal replacement therapy during their ICU stay. The risk of ARF appears to be higher in CICPs compared to other critically ill patients (*Acute Renal Failure After Cancer Treatment*, n.d.).

5.2 Discussion

This discussion interprets the key findings of the study on renal insufficiency among patients managed for 5 major cancers at the Kenyatta National Hospital (KNH), structured explicitly around the pre-specified research objectives. The results reveal a complex interplay between demographic factors, oncological disease profiles, therapeutic interventions, and renal function.

5.2.1 Demographic Characteristics and their Association with Renal Insufficiency

The study cohort of 330 patients reflected a typical oncology population with a median age of 57 years and a slight female predominance (56.1%). The age distribution was notably skewed toward older adults, with 84.2% of participants over 40 years and 41.5% over 60 years. This demographic profile is significant, as age is a well-established, non-modifiable risk factor for declining renal function due to physiological processes such as glomerulosclerosis, reduced renal blood flow, and diminished functional nephron mass.

The statistical analysis robustly confirmed this expected relationship. In the bivariate model, patients aged over 60 years had 2.16 times the odds (OR 2.16, 95% CI 1.10–4.35) of having renal insufficiency compared to those aged 40 or younger. This association persisted and was slightly strengthened in the multivariable analysis after adjusting for potential confounders (aOR 2.33, 95% CI 1.16–4.87). The biological plausibility is strong: the aged kidney has a reduced capacity to withstand additional insults, such as those posed by cancer itself (e.g., dehydration, hypercalcemia, obstructive uropathy) or its treatments (e.g., nephrotoxic chemotherapy, contrast agents). Consequently, advanced age must be considered a primary risk stratifier for renal impairment in this clinical setting. The higher odds of renal insufficiency among older patients is 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).

Declining renal function is common among the elderly. As individuals age, kidney mass decreases, and age-related reductions in renal blood flow lead to a gradual loss of functional nephrons. This reduction in kidney cortical mass signifies a decrease in overall renal function, with lower glomerular filtration and diminished tubular activity. The renal function typically declines by approximately 1% per year after age 30–40, so by age 70, it may have decreased by as much as 40% (Launay-Vacher, 2016). The lack of a

significant association with gender suggests that sex-linked biological factors are less influential than the universal process of age-related renal decline in determining the prevalence of renal insufficiency within this oncological cohort.

5.2.2 Major Cancer Types, Histological Classes, Clinical Stages, and their Association with Renal Insufficiency

The study focused on five most prevalent cancers at KNH: breast, cervical, prostate, esophageal and colorectal cancers. A critical and concerning finding was the profound late-stage presentation of disease. A staggering 86.7% of patients were diagnosed at Stage III or IV, with over half (54.9%) already at Stage IV. In contrast, only five patients (1.5%) were diagnosed at stage I. This pattern of advanced disease at diagnosis has major implications for both oncology and nephrology outcomes. Late-stage cancers are often associated with a higher systemic burden, increased risk of metabolic complications (e.g., tumor lysis syndrome), and a greater likelihood of requiring aggressive, potentially nephrotoxic, multi-modal therapies. Histologically, adenocarcinoma predominated in colorectal and prostate cancers, while squamous cell carcinoma was commonest in cervical and oesophageal cancers, consistent with known biological patterns.

Despite this, the analysis revealed that neither the specific cancer type, histological classes nor its clinical stage at diagnosis was a statistically significant independent predictor of renal insufficiency in the final adjusted model. This is a nuanced and important finding. It suggests that while advanced cancer may contribute to renal stress, the *direct* impact of tumor histology or burden on glomerular filtration rate (GFR), as measured in this cross-sectional study, may be overshadowed by other factors like age and specific drug toxicities. However, a notable trend was observed: patients with cervical cancer showed nearly double the odds of renal insufficiency compared to those with breast cancer (OR 1.97, 95% CI 0.99–4.00, p=0.056). This borderline significance warrants hypothesis generation. It may be related to locoregional anatomy, where advanced cervical disease could cause ureteral obstruction, or to specific treatment paradigms. 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 tumors also lead to obstructive uropathy (Habas et al., 2023). Based on this, cancers close to the kidneys can be considered the highest culprits in renal failure.

5.2.3 Main Treatment Modalities and Their Relationship with Renal Insufficiency

The treatment landscape was characterized by a high rate of active (89.7%) and multi-modal (88.2%) therapy. Chemotherapy was central, with platinum derivatives (39.4%), taxanes (20.6%), and antimetabolites (15.8%) being most frequently administered. Platinum compounds such as cisplatin are known nephrotoxins through tubular injury, renal vasoconstriction, and oxidative stress. Surprisingly, platinum use was not significantly associated with renal insufficiency in this study. This could be explained by: dose modification protocols, hydration practices, selective use in fitter patients, survival bias, pre-treatment renal assessment excluding high-risk patients.

A notable and novel finding was that use of taxanes was associated with lower odds of renal insufficiency, both before and after adjustment (aOR 0.47; 95% CI 0.25–0.85). Taxanes are not primarily nephrotoxic, and the protective association may reflect confounding by indication, where patients selected for taxane therapy may be healthier or younger. Similar to our study, a retrospective cohort study by Kobayashi et al (2019) suggests that docetaxel may be a viable treatment option for non-small cell lung cancer (NSCLC) patients with moderate to severe, non-dialysis dependent chronic kidney disease (stage 3b or higher), as it demonstrated no significant increase in hematologic or non-hematologic toxicities, no accelerated decline in renal function, and similar survival outcomes compared to patients with better kidney function. Excretion of taxane products are majorly through the liver. Currently, anthracyclines, taxanes, and trastuzumab are not regarded as nephrotoxic, and existing guidelines do not recommend dose adjustments for patients with renal impairment (Albini et al., 2018).

Numerous recent comprehensive reviews are available in the literature on the potential nephrotoxicity and renal processing of cancer chemotherapy drugs. Extensive information exists on classic cytotoxic drugs such as cisplatin, carboplatin, and oxaliplatin; alkylating agents like bendamustine, cyclophosphamide, ifosfamide, nitrosoureas, temozolomide, and melphalan; anti-tumor antibiotics such as mitomycin C and bleomycin; anti-metabolites like methotrexate, pemetrexed, capecitabine, and gemcitabine; vinca alkaloids including vincristine, vinblastine, and vinorelbine; taxanes such as paclitaxel, docetaxel, and cabazitaxel; and the topoisomerase inhibitor irinotecan (Lameire, 2013).

The use of the aromatase inhibitor letrozole/anastrozole showed a strong, albeit marginally non-significant, association with renal insufficiency (aOR 4.81, 95% CI 0.99–34.65, p=0.067). 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). Surgery, radiotherapy and immunotherapy also showed no significant independent associations with renal insufficiency.

5.2.4 Prevalence of Renal Insufficiency in Cancer Patients

A cornerstone finding of this study is the high prevalence (38%, 95% CI 33–44%) of renal insufficiency (eGFR <90 mL/min/1.73m²) among cancer patients at KNH. This figure is substantially elevated compared to general population estimates and highlights a major comorbidity burden. The severity was predominantly mild (Stage G2, eGFR 60-89, in 29.4% of the total cohort), but 7.6% of patients had moderate-to-severe impairment (eGFR <45). This high prevalence has immediate clinical implications: it affects the pharmacokinetics and safety profiles of many anticancer drugs (e.g., methotrexate, carboplatin, bleomycin), influences surgical risk, and can limit therapeutic options. It underscores the non-negotiable requirement for routine and serial assessment of renal function in all cancer patients, not just those receiving known nephrotoxins. The finding transforms renal insufficiency from a peripheral concern to a central component of

comprehensive oncology care.

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). 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 we have 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 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. (2005) 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 study populations e.g., demographic characteristics e.g., age, the type of cancer or even the stages of cancer at the time of the test. 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.

In the current study, stage 2 renal insufficiency was the most prevalent followed by stages 3a, 3b, 4 and 5. Similar findings of the severity of renal insufficiency among cancer patients have been reported in Brazil (Pontes et al., 2014) and in Belgium (Launay-Vacher, Oudard, et al., 2007). Rajabu et al. (2024) in a study of renal failure among cancer patients also reported that most of the patients studied had stage 2 renal failure followed by those with stage 3.

In agreement with this study, the estimated chronic kidney disease (stages 3-5) has been put between 11% and 13% which is close to our finding of 9.1% (Lees et al., 2023).

According to Lee et al., understanding the connection between chronic kidney disease (CKD) and multimorbidity is essential for enhancing patient outcomes. Risk factors for CKD and cancer overlap; however, CKD occurs more frequently in cancer patients than in the general population, significantly influencing treatment choices and outcomes (Lees et al., 2023).

5.3 Strengths and Weaknesses

5.3.1 Strengths

The study focused on common cancers with high public health relevance. Use of standardized CKD-EPI equation and inclusion of both inpatients and outpatients' data. There was multivariable adjustment for confounding. Lastly, the study met the calculated sample size hence the power of the study was not affected.

5.3.2 Weakness

This is a single-centre study and therefore the findings may not be generalised to other centres. This is cross-sectional study which looks at renal insufficiency at a given point of time. The study is conducted at national referral hospital in the major city. Therefore, the finding may not be representative of what is happening in the rural countryside. There are many components of measuring renal insufficiency although the current study looked at only eGFR to assess renal function. There are relatively small subgroup sizes for some treatments. Exclusion of patients without full labs may bias estimates of research findings

5.4 Conclusion

Renal insufficiency is highly prevalent among adult cancer patients at KNH, affecting more than one-third of patients. Increasing age strongly predicts renal dysfunction, while taxane chemotherapy appears to be associated with reduced renal risk. Routine renal assessment and age-tailored cancer treatment planning are therefore essential components of comprehensive oncology care in Kenya.

5.5 Recommendations

1. Routine renal function monitoring should be standard in oncology care. Older patients warrant closer renal surveillance.
2. Chemotherapy selection should incorporate renal risk assessment.
3. Early cancer detection strategies remain urgently needed. Most patients are diagnosed in late stage of cancer in this research.
4. We recommend Large multicenter cohorts longitudinal follow-up study to assess renal decline over time.
5. We recommend similar study that takes into account different criteria of assessing renal disease: albuminuria or urine albumin-to-creatinine ratio, renal tubular abnormality and associated electrolyte disorder and finally abnormalities in urine sediment, histology, or imaging suggestive of kidney damage.

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APPENDICES

Appendix I: Study Timelines

ACTIVITY	MARCH- JUNE 2024		JULY- SEP 2024		OCT 2024- JAN 2025		FEB 2025- MAR 2025	
Research Proposal and Preparatory Phase								
Data Collection and Storage								
Data analysis and Thesis Write-up								
Submission of Thesis								

Appendix II: Budget

CATEGORIES		PRICE
ITEM	JUSTIFICATION	KES
1. Data collection instruments and related expenses	Computer maintenance, internet bundles, pen and other consumables	20,000.00
2. Travel expenses	Daily commuting for research activity for one month	10,000.00
4. Printing and binding	Printing of questionnaires, consent forms, Thesis booklet	10,000.00
6. Research assistants	30 days each assistant given 2000.00 per day	120,000.00
7.Training of research assistants	Accommodation, travel and allowances 5000.00 per day for 3 days	30,000.00
Sub-Total		**190,000.00**
10% Contingency		19,000.00
Grand-Total		**209,000.00**

Appendix III: Map of Study Location

Appendix IV: Consent to Participate in Research

Consent Form Section A: Study Information

Study Title: RENAL INSUFFICIENCY AND ASSOCIATED CLINICAL, DEMOGRAPHIC AND TREATMENT CHARACTERISTICS AMONG CANCER PATIENTS AT KENYATTA NATIONAL HOSPITAL, NAIROBI, KENYA.

Principal Investigator: Dr Gabriel Dokata Qalicha

Co-investigator(s): Dr. Beatrice Wangari Ndege and Dr. Namasaka Philemon

Role of co-investigators: Supervision research process and moral support

Institution: Jomo Kenyatta University of Agriculture and Technology

Statement of the Researcher

I request you to participate in a research study. The information in this form explains what participation in the study entails. Please, listen carefully as I read this form. You are free to ask questions about what I will ask you to do, the risks involved, the benefits, your rights as a volunteer or anything in this form that may not be clear to you. In a process known as informed consent you decide whether or not you would like to participate in the study. If you agree to take part in the study after we have described it to you and having answered any questions you have to your satisfaction, we will give you a signed copy of this form for your records.

Purpose of the Study

The purpose of this study is to assess the prevalence of renal insufficiency and associated clinical, demographic and treatment factors among cancer patients at Kenyatta national hospital, Nairobi, Kenya. The finding from this study will help in early identification and institution of preventive measures in kidney disease progression in cancer patients. This

will enhance joint contribution from health care workers, government policy makers, healthcare administrators and other stakeholders to reduce morbidity and mortality related to renal insufficiency in cancer patients and optimizing healthcare delivery to patients.

Study site: KNH, Oncology wards and clinics

Study population: Cancer patients above 18 years and are being managed at KNH Oncology wards and clinics

Study Procedure

The study will be carried out in KNH in Nairobi. I shall engage trained research assistants to work with me so as to assess the prevalence of renal insufficiency in cancer patients. If you agree to participate in the study, we will interview you at the hospital and also obtain some of your information from medical files. The interview will take about 10 to 15 minutes.

Risks, Stress and Discomforts

This study does not put you at any risk. However, answering the questionnaire will take about 10 to 15 minutes.

Benefits of Participating in the Study

Your participation will help us assess the prevalence of renal insufficiency and associated clinical, demographic and treatment factors among cancer patients at Kenyatta national Hospital. Feedback and recommendation from this study may positively contribute to care of patient in future and help in mitigating kidney disease in cancer patients. However, there is no financial benefit of any sort for the participants. Participation is purely voluntarily.

Volunteerism and other Information

Your participation in this study is absolutely voluntary and you may decide to withdraw your participation before or during the interview without any consequences. It is still possible to decline to participate even after signing this consent form. Information generated from this study will be used for the purpose described in this consent form. We would like to reassure you that the data and any publication from this study will not contain information that will reveal your identity as a participant in compliance to data protection act 2019. Only the investigator and study staff will have access to information that link your name on the consent form you have signed or put your mark on and your study number. We will keep information you give confidential. Should you have any question about the study, please feel free to get in touch with.

Gabriel Dokata Qalicha

_____ _____ _____

Name of Researcher Signature Date

Consent Form Section B: Statement of the Participant

The purpose of the study has been clearly explained to me. I consent to participate in this study. I have been accorded the opportunity to ask questions. I understand that my participation in this research will expose me to no risk. I understand that my identity will be kept confidential. Data will be coded such that my identity will not be compromised at any time nor will any key with participant names be available to anyone other than the investigator of this research and the academic supervisors. I understand that if I need additional information or have further questions, I will reach the investigator, co-investigators and affiliated institution through the given contacts.

_____ _____

Name of Participant Signature Date

Contact information

In case of any issues or challenges related to this study, please contact me on +254 725903184 or any of my Supervisors Dr. Namasaka Philemon +254 721689085/ Dr. Beatrice Wangari Ndege +254 722865819 or /UON ERC Secretariat on uonknherc@uonbi.ac.ke or +254 721 257746, (020) 318262 Ext.28250.

Thank you for sparing your precious time dedicated to participating in this study exercise.

Appendix V: Data Collection Questionnaire

Date……..

Patient unique no. …….

Department (ward/ clinic)…….

In patient/ward number……..

Outpatient/clinic number……...

Name of Hospital ……

1. **Demographic information**
   a. Date of birth……..
   b. Gender……...
   c. BMI…….
2. **Cancer diagnosis and clinical staging at the time of diagnosis**

a. Cancer diagnosis……..
b. Histological type……..
c. Clinical stage of cancer at the time of diagnosis.

Stage 1…….

Stage 2…….

Stage 3…….

Stage 4…….

Stage 5…….

3. Renal insufficiency on various treatment modalities

a. What are patient latest creatinine level (in last 2 weeks)

……..

b. Patient eGFR by CKD- EPI in ml/min/1.73m2

1. More than 90 ……..
2. 60- 90 ……..

3a. 45- 59 ……...

3b. 30- 45 ……..

4. 15- 29 …….
5. Less than 15/ on dialysis/ transplant …….....

4.Treatment modalities currently on

4.1 NO…….

A. If No, give reason…….

4.2 Yes…….

B. If Yes, which one

1.2.1 Chemotherapeutic agents

a) ……..

b) ……..

c)……

d)……

e) ……

f) ……

1.2.2 Surgery done

I. No…….

II. Yes…….

If yes, surgery is done for

a. Tumor removal …….
b. Palliative/ de- bulking ……
c. Palliative

…….

1.2.3 Hormonal anti- cancer therapies

a) ……..

b) ……..

c)…….

d)…….

e) ……..

f……

1.2.4 Radiotherapy

a. Yes……

b. No……..

1.2.5 Immunotherapeutic agents

a) ……..

b) ……..

c)……

d)……

e) ……

Thank you for your participation