



Original Article

Histological Profile of Kidney Malignancies at a Tertiary Hospital in the Ashanti Region of Ghana; A 9-Year Review

Paul Poku Sampene Ossei^{1*}, Benedict Mawuli Agagli¹, William Gilbert Ayibor², Nicholas Niako¹, Emmanuel Asante¹

¹Department of Pathology, SMD, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana

²Department of Molecular Medicine, SMD, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana

Abstract

Background: Kidney cancer is the 14th most prevalent cancer worldwide, however, it is relatively less common in Ghana compared to other countries in northern and southern Africa. This study presents the profile and prevalence of kidney cancer cases in Ghana. **Methods:** The study analyzed the histopathological data of 321 cases of kidney cancer obtained from pathology records at Komfo Anokye Teaching Hospital, Ghana. **Results:** Most of the kidney malignancies were Wilm's tumor (WT) (nephroblastoma), accounting for 44% ($n = 141$) of all cases, followed by renal cell cancer (RCC) (40%, 127), kidney lymphoma (11%, 37), urothelial cancer (4%, 13), and sarcoma (1%, 3). Children were most affected by the disease, especially WT. Age distribution of the disease was right skewed, and trend analysis showed a slight decline since 2014. **Conclusion:** WT is the most common type of kidney cancer in Ghana followed by RCC. The implementation of Ghana's "National Strategy for Cancer Control 2012–2016" has led to a large decrease in the occurrence of the disease in the country.

Keywords: Abdominal mass, cancer, histopathological, kidney malignancy, urothelial cancer, Wilm's tumor

INTRODUCTION

The kidney as an organ is prone to many disorders, including acute kidney injury, kidney cysts, kidney stones, uremia, nephritis, kidney infections, and renal tumors (kidney cancer). Diabetes and high blood pressure have been shown to increase the risk of kidney disease.^[1]

Kidney cancer is the 14th most common cancer worldwide^[2] and is caused by the uncontrolled growth of cells in one or both kidneys. Tumors can be malignant, indolent, or benign. Both malignant and indolent tumors are cancerous; however,

malignant tumors can also metastasize to other parts of the body while indolent tumors rarely spread. Benign tumors can grow but will not spread.^[3] There are several types of kidney cancer. Renal cell cancer (RCC) develops in the proximal renal tubules that make up the kidney's filtration system. This type of cancer is the most common type of kidney cancer, which can occur at any age but occurs mostly in adults, accounting for about 85% of adult cancer diagnoses.^[4] It also accounts

Address for correspondence: Dr. Paul Poku Sampene Ossei,
'Department of Pathology, SMD, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana.
E-mail: possei.chs@knust.edu.gh

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for 80%–85% of malignant kidney tumors, and males are more predisposed than females.^[3–6] Around 30,000 new RCC cases are diagnosed in the US each year. Urothelial cancer, also termed transitional cell cancer, also affects the kidneys. It begins in the area of the kidneys where urine collects before moving to the bladder, called the renal pelvis (lined by urothelial cells).^[7] Earlier studies have shown that urothelial cancer occurs more commonly in men than in women with the ratio of 3:1.^[8] The abuse of compounds containing phenacetin has been reported to increase the risk of urothelial cancer of the renal pelvis.^[8] This type of kidney cancer has been reported to account for 10%–15% of kidney cancers diagnosed in adults, and it is treated in the same manner as for bladder cancer because both types start from the same cells.^[3] Sarcoma of the kidney is rare and develops in the soft tissue of the kidney; the thin layer of connective tissue surrounding the kidney called the capsule.^[3] Sarcoma of the kidney is associated with squamous metaplasia of the renal pelvis, renal calculi, or infection.^[9] The tumors are aggressive in nature and usually have a poor prognosis, but is rare in the renal pelvis.^[10] A study by the National Cancer Institute (NCI) reported that about 15% of cancer diagnoses in children under 20 years of age are sarcomas, and that approximately 11,280 new cases of soft-tissue sarcoma are diagnosed in the US each year with almost 35% of them dying of the disease yearly.^[11] Wilm's tumor (WT) is the most common pediatric renal tumor, and accounts for about 90% of kidney cancers in children.^[12] An abdominal mass, swelling and pain, and other signs such as blood in urine and high blood pressure are associated with WT. Congenital anomalies and other clinical conditions have been found to be associated with children diagnosed with this type of kidney malignancy.^[13,14] The disease occurs equally in both genders,^[15] and it is most commonly treated with radiation therapy and chemotherapy.^[3] The prevalence of WT has been reported to be lower in Asian countries than in the US.^[15] Lymphoma is a malignant tumor caused by lymphoid cell proliferation.^[16] Although the kidney is not a lymphoid organ, kidney lymphoma can appear as a lone tumor mass in the kidneys with enlargement of the kidneys in connection with enlarged lymph nodes, called lymphadenopathy.^[3,17] Primary renal lymphoma accounts for 0.7% of all extranodal lymphomas, with clinical presentations including abdominal mass, fever, and weight loss.^[16,18] Most cases are diagnosed postmortem as part of a disseminated disease.^[17]

A study on kidney carcinoma by the American Institute for Cancer Research reported over 400,000 new cases of the disease in 2018. It is the 9th most common cancer in men, and 14th in women.^[2] *African*. com and other studies have reported that age is a significant risk factor for cancer. A recent study by Capitanio *et al.* showed that Northern America and Western Europe have high cumulative incidence and mortality rates of kidney cancer, but that the rates are very low in Africa.^[19] In Ghana, the Ministry of Health in their “National Strategy for Cancer Control 2012–2016” study reported that 16,600 cases of cancer occur annually in

the country, yielding an age-standardized rate of 109.5 cases per 100,000 persons.^[20]

The kidney cancer statistics reported in 2018 by the American Institute for Cancer Research did not list a single African country among the top 20 countries, not because the prevalence of the disease is low in the continent, but due to a lack of available data.^[2] A systemic review study on kidney cancer in Africa by Atanda and his colleagues reported an underestimation of RCC accounting for about 0.3% of all adult cancers due to insufficient record keeping which hinders comprehensive data gathering.^[21] The need for accurate information on the epidemiology of kidney cancer has become important for planning and improving treatment strategies and resource allocation to target agents.^[22] Therefore, the aim of this study was to investigate the profile and prevalence of the various kidney cancer types in Ghana, and also to investigate the relationship between the patient's gender and diagnostic specimen, and discuss variations in the pathology.

METHODS

Ghana has two specialized centers for treating kidney diseases; Korle-Bu Teaching Hospital in Accra, and Komfo Anokye Teaching Hospital (KATH) in Kumasi. KATH is the major referral hospital that serves the whole of Ashanti and its surrounding regions. Secondary data extracted from the daily record books of KATH were used in this study. Histopathological data of 321 cases of kidney cancer from 2009 to 2017 (9 years) were obtained. The data extracted included the patients' demographics, specimens, clinical diagnoses, and histopathological reports, which were compiled and analyzed using MS Excel 2016 and Statistical Package for Social Sciences (SPSS, IBM, Chicago, USA). Waiver of informed consent was approved by the Committee. The Committee on Human Research Publications and Ethics (CHRPE) of the School of Medicine and Dentistry, Kwame Nkrumah University of Science and Technology, gave approval for the study (no: CHRPE/AP/323/19) on the May 22, 2019.

RESULTS

General description

Of the 321 enrolled cases with kidney malignancies, 49% ($n = 157$) occurred in males and 51% (164) in females. The average age was 17 years, with a modal age of 3 years in 35 cases. The youngest patient was a 3-month-old girl diagnosed with nephroblastoma (WT) in the left kidney, and the oldest patient was a 97-year-old man diagnosed with recurrent nephroblastoma (WT) in both kidneys. The general age distribution was skewed to the right, as the mean age (17 years) was greater than the median age (9 years) and were both greater than the modal age (3 years). More of the kidney cancer cases were diagnosed among children. The most common type of kidney cancer was WT (141 cases, 44% of all cases), followed by RCC (127, 40%), lymphoma (37, 11%), urothelial cancer (13, 4%), and sarcoma (3, 1%). The left

kidney was more affected (175, 54%) than the right kidney (87, 27%), and 44 (14%) cases involved both kidneys (the data of 15 (5%) cases were not recorded). Of the cancers in the left kidney, 46% were RCC, 40% were WT, 10% were lymphoma, 3% were urothelial cancer, and 1% were sarcoma. All three cases of sarcoma were diagnosed in the left kidney. Of the cases diagnosed in the left kidney, 49% occurred in males and 51% occurred in females. Of the cancers in the right kidney, 55% were WT, 29% were RCC, 9% were lymphoma, and 7% were urothelial cancer. Of these cases, 59% occurred in females and 41% in males. The distribution is summarized in the Venn diagram [Figure 1].

Gender distribution

Of the total of 321 cases, 157 (49%) were male and 164 (51%) were female. Of those with WT ($n = 141$), 49% were male and 51% were female. Although the number of cases of kidney lymphoma (37) and RCC (127) were different to WT (141) they had equal gender rates. One (33%) of the sarcoma cases was diagnosed in a male and two (67%) were diagnosed in females. On the other hand, urothelial cancer (13) had a higher rate in males (54%) than in females (46%). This is summarized in Figure 2 with males in green and females in orange.

Wilm's tumor

As mentioned above, the most common type of kidney cancer was WT (141 cases, 44% of all cases). Of these cases, 124 (88%) were diagnosed in children under 10 years of age, with the same distribution in males and females (62 males and 62 females). Eleven (8%) cases occurred in people between 10 and 19 years of age, including six in males and five in females. One case occurred in the age range 20–29 years and one in the age range 30–39 years, both in females. Two cases occurred in the age range 40–49 years, and both were females. No cases of WT were diagnosed among people aged between 60 and 69 years, but one case occurred in a male patient aged above 69 years. The distribution of WT affecting children was significant and is shown in Table 1.

Renal cell cancer

A total of 127 patients were diagnosed with RCC. Most cases of RCC were diagnosed in patients aged between 10 and 19 years ($n = 41$, 32%; 22 men and 19 women), followed by those aged <10 years ($n = 21$, 17%; 10 males and 11 females), 40–49 years ($n = 16$, 13%; 6 males, 10 females), 20–29 years ($n = 14$, 11%; 7 males and 7 females), 30–39 years ($n = 11$, 9%; 6 males and 5 females),

50–59 years ($n = 10$, 8%; 5 males and 5 females), 60–69 years ($n = 8$, 6%; 3 males and 5 females), and >69 years ($n = 6$, 5%; 3 males and 3 females). The summary of frequencies of each age range (indicated in red bars) and gender frequencies (indicated in blue bars) for males and light green bars for females respectively to each age range is depicted by the figure 3 below.

Kidney lymphoma

Lymphoma was the third most common type of kidney cancer among Ghanaians ($n = 37$, 12% of all cases). Most ($n = 21$, 57%) cases were diagnosed among children <10 years, followed by 10–19 years ($n = 12$, 32%), 20–29 years ($n = 1$, 3%), and >69 years ($n = 1$, 3%). No kidney lymphoma

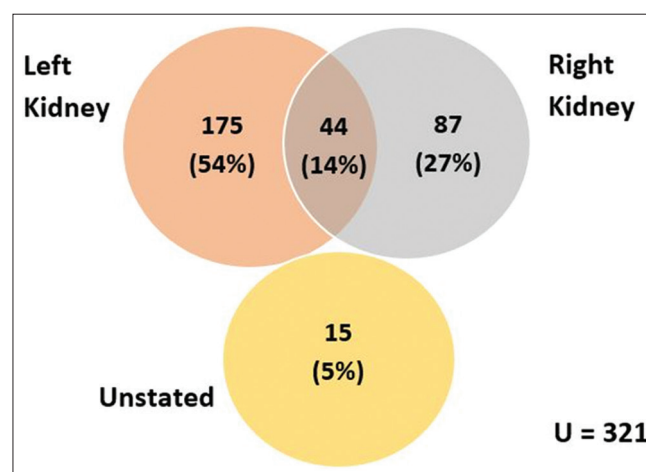


Figure 1: A venn diagram showing specimen distribution

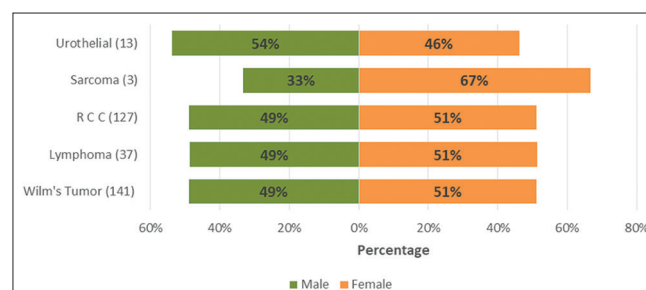


Figure 2: Gender distribution of the cancers

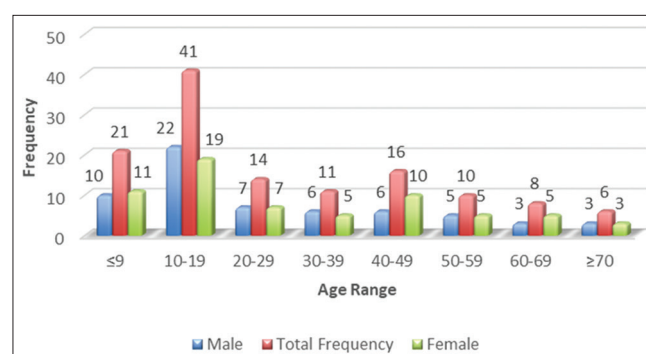


Figure 3: Age range and gender distribution of renal cell cancer

Table 1: Age and sex distribution of Wilm's tumor in children

Age group	Males	Females	<i>n</i>
0-4	36	44	80
5-9	26	18	44
10-14	5	4	9
15-19	1	1	2
<i>n</i>	68	67	135

n: Total frequency

cases were diagnosed among the age ranges 30–39, 40–49, 50–59, and 60–69 years. Overall, 89% of the kidney lymphoma cases occurred among patients <20 years of age. The bar chart [Figure 4] shows the total frequencies of kidney lymphoma per age range in red and of gender per age range; males in blue and females in light green.

Urothelial cancer and sarcoma

These two types of kidney cancer were the least common among. A total of 13 urothelial cancers were diagnosed and three sarcomas. Of the urothelial cancer cases, two occurred in children <10 years of age, and they were all males. Four cases occurred in patients aged 10–19 years (2 males, 2 females), two in those aged 20–29 years (both males), two in those aged 40–49 years (1 male, 1 female), and one in a patient aged 60–69 years (female).

Of the three cases of sarcoma, one was aged < 10 years (male), one was aged 40–49 years (female), and one was aged 50–59 years (female). All are presented in Table 2.

Yearly trend plot

There were only seven cases of kidney cancer in 2009, with a drastic increase in 2010 to 29 cases, and then 32 cases in 2011 and 42 cases in 2013. The highest number of cases ($n = 51$) was recorded in 2014, after which the number of cases decreased in 2015 to 45 and continued to decrease to 38 and then 36 cases in 2016 and 2017, respectively. Figure 5 gives a summary of the yearly trend of recorded kidney cancers.

Association between gender and kidney malignancy

There were differences in the occurrence of cancer in the left and right kidneys between the male and female patients. Of the 54% of cases diagnosed in the left kidney only, 49% occurred in males and 51% in females. In comparison, of the 27% of cases diagnosed in the right kidney only, 41% occurred in males and 59% in females, so that the rate of cancer in the right kidney in females was higher than that in the left kidney.

A Chi-square test was done on 306 valid data to assess the correlation of gender with site of malignancy (left or right kidney). This will provide information regarding the decision on kidney donation programs and others.

As shown in Table 3, the Pearson Chi-Square there is significant evidence that, there is a significant association between a patient's gender and the specimen involved in kidney cancer diagnosis, especially in the Ghanaian geography.

DISCUSSION

Of the 321 cases of kidney cancer in this study, there was a slight female preponderance (51% vs. 49% in males). The gender ratio of the disease in Ghana is approximately 1:1, which agrees with trends observed in relative studies worldwide.^[21] Although most previous studies have reported that RCC is the most prevalent type of kidney cancer, we found that WT was the most common type in our Ghanaian

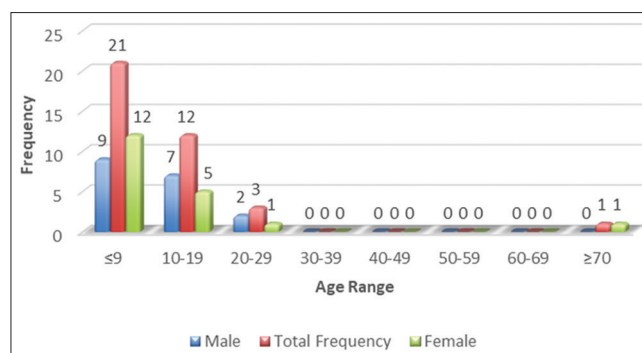


Figure 4: Age range and gender distribution of kidney lymphoma

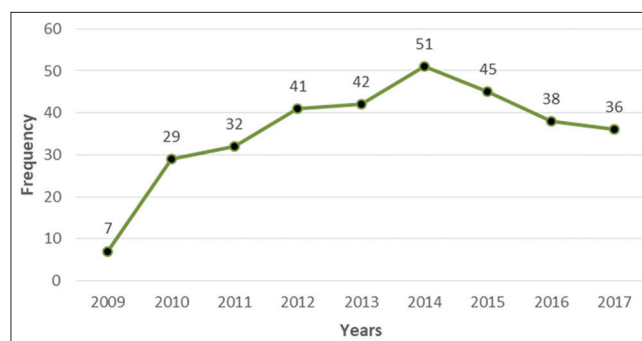


Figure 5: A plot of yearly trend of kidney cancer incidence in the Ashanti region

population, accounting for 44% (141) of all cases studied. In addition, 88% of these cases were diagnosed among children below 10 years of age, and 8% among young children between 10 and 19 years. These findings support those of other studies in that the disease is a childhood cancer. The American Cancer Society (ACS) has reported that 90% of kidney cancers in children are WT. Even though the ACS estimates that WT occurs slightly more often in females than in males,^[23] we found an equal distribution in both genders. As the disease exhibits random behavior in its occurrence, its causes are broadly grouped as syndromic and nonsyndromic, with syndromic causes of WT being due to genetic mutations affecting the kidney. Most WT cases develop from nephrogenic rests, which are fragments of tissue in or around the kidney that develop before birth and become cancerous after birth.^[24,25] Other studies have reported that genetic differences influence the treatment of children with WT. For example, the treatment of WT in patients with certain changes in chromosomes 1 or 16, seem to be more likely to recur after treatment.^[26] Ninety percent of cases of WT are treated based on the stage of cancer and histology; whether favorable or anaplastic. Other factors such as the child's age, chromosome changes, and tumor size also influence treatment.^[23]

RCC was the second-most common type of kidney cancer in this study, and it was more common among the adults as expected. Of the 127 cases, only 17% were diagnosed among children below 10 years of age, 32% among people between 10 and 19 years of age, and 51% among people older than

Table 2: Age range distribution of urothelial cancer and sarcoma

Age range	Cancer type					
	Urothelial			Sarcoma		
	Male	Female	Frequency (%)	Male	Female	Frequency (%)
0-9	2	0	2 (15)	1	0	1 (33)
10-19	2	2	4 (31)	0	0	0 (0)
20-29	2	0	2 (15)	0	0	0 (0)
30-39	0	0	0 (0)	0	0	0 (0)
40-49	1	1	2 (15)	0	1	1 (33)
50-59	0	0	0 (0)	0	1	1 (33)
60-69	0	1	1 (8)	0	0	0 (0)
>70	0	2	2 (15)	0	0	0 (0)
Total	7	6	13 (100)	1	2	3 (100)

Table 3: Chi-Square Test Output

	Value	df	Asym. Sig. (2-sided)
Pearson Chi-Square	6.390 ^a	2	.041
Likelihood Ratio	6.475	2	.039
Linear-by-Linear Association	1.175	1	.278
N of Valid Cases	306		

^a0 cells (0.0%) have expected count less than 5. The minimum expected count is 21.86

19 years of age. This is consistent with other studies which have reported that RCC is the most common adult kidney malignancy,^[27] usually occurring from the 5th to 7th decades of life as with any other cancers and accounting for 80%–85% of malignant kidney tumors, with no clear gender preponderance.

Recent studies of the predominance in early age have suggested associations with changing lifestyles and higher exposure to hazardous work environments among younger Africans.^[21] The strongest risk factors for RCC include cigarette smoking, obesity, and hypertension. People with diabetes mellitus and who consume alcohol have also been estimated to account for almost 50% of cases,^[28,29] even though Bellocchio *et al.* reported that moderate consumption of alcohol had a protective effect against RCC.^[30] The long-term use of nonsteroidal anti-inflammatory drugs has also been suggested to be a risk factor for RCC.^[31] The 5-year survival rate of RCC has been reported to be 65%–90%.^[27] In other countries such as Nigeria, patients managed with or without resection, chemotherapy, radiotherapy, and adjuvant therapy have been reported to have a shorter survival rate of 13.6%–56% for 1–5 years.^[21] The gender ratio of RCC in the current study was 1:1, which is relatively low in Africa, where it has been reported to be 1:4 in northern Africa and 1:9 in southern Africa.^[32] The disease is heterogeneous with multiple tumor types, each derived from various parts of the nephron, epithelium or renal tubules, and possessing different genetic characteristics and histological features. Moreover, 72% of the RCC cases were of the clear cell histological subtype and

22% were papillary RCC. The clear cells in the epithelium of the proximal convoluted tubules appear heterogeneous with areas of necrosis and hemorrhage. Papillary RCC, which is the second-most common RCC histologic subtype, macroscopically contain areas of hemorrhage, necrosis, and cystic degeneration. It is histologically characterized by a predominantly papillary growth pattern, while the tumor papilla consists of a fibrovascular core with stromal aggregates of foamy macrophages with cholesterol crystals. Other histologic subtypes of RCC such as chromophobe RCC, which involves macroscopically well circumscribed, solid, tan-brown tumors with a mildly lobulated surface and histopathologically characterized by large polygonal cells with prominent cell membranes and others such as cystic solid, collecting duct, medullary^[33-37] are uncommon in Ghana. Maintaining normal body weight has been reported to reduce the risk of RCC.^[38] Treatment depends on the stage, and may require removal of the entire kidney or the affected part. Apart from surgery, chemotherapy and immunotherapy are both standard treatment procedures, and the use of radio waves to destroy the tumor or freezing it have also been reported to be effective.^[39]

The third most common type of kidney cancer in this study was kidney lymphoma, which was diagnosed in 37 cases over the 9-year period. Of these cases, 35 (95%) were Burkitt lymphoma, thus non-Hodgkin lymphomas. In Ghana, the disease is mostly seen in people below the age of 30 years, and 57% of all lymphoma cases in this study were diagnosed in children aged 6–8 years with no difference in gender distribution. The 5-year relative survival rate of people with kidney lymphoma was estimated to be 71% in a study by the ACS.^[20] However, kidney lymphomas in Ghana are of more aggressive types, resulting in a shorter survival^[40] Ghanaian victims of the disease have a lower survival rate, which is influenced by the stage of disease and kidney lymphoma type, as evidenced in a recent case study of a 25-year-old girl.^[40] A global study reported that 4.3 million people had non-Hodgkin lymphoma in 2015, of whom 7% died, highlighting the benefit of detecting the disease early.^[41,42]

Sarcoma and urothelial cancer were very uncommon in this study. All of the 13 urothelial cancer cases were diagnosed in people below 20 years of age. More of the urothelial cancer cases occurred in men (7 in males vs. 6 in females), although the difference was not significant. Malignancies of squamous cell cancer accounted for all of the urothelial cancer cases in this study. They were often multifocal on pathology and presented with a papillary pattern. Some studies have reported that urothelial cancer occurs at a ratio of 1:3:50 in the renal pelvis, ureter, and bladder, respectively, and that urothelial cancer is more common in whites than in blacks, with a strong correlation with the duration and amount of cigarettes a person smokes.^[43] In this study, there were three cases of sarcoma, of whom two were aged 40–60 years and were females. They were all angiosarcomas and were graded as intermediate after a microscopic view. The grade of tumors has been reported to have an effect on the survival rate of sarcoma patients. In other countries such as the US, sarcoma accounts for 0.3% of all cancer deaths with a 5-year survival rate estimated to be 80.8%. The ACS also reported that there were 12,750 new soft tissue sarcoma cases of whom 41% died in 2019.^[44,45] As of 2019, research is ongoing to identify new medications to treat sarcoma. A possibility will be the use of immune checkpoint inhibitors such as anti-PD1, anti-PDL1, and anti-CTLA4 agents (immunotherapy) to treat sarcomas,^[46] even though metastasized sarcoma is currently been treated with chemotherapy.

Although there were over 400,000 new kidney cancer cases in 2018 with a high incidence in countries such as the US, trend analysis in the current study showed that it has been decreasing in Ghana since 2014. The health ministry reported in their 2012–2016 cancer action plan that low awareness can be attributed to the earlier high number of cancer cases in the country.^[20] In achieving Ghana's sustainable development goals, activities such as organizing cancer awareness campaigns with free health screening have contributed greatly to the early detection of the disease, and this has influenced the rate of cancer deaths in general among the Ghanaian population in recent years. Documenting cancer cases to establish a cancer registry has also helped on the basis of research, surveillance, and delivering cost-effective interventions. It has also helped to improve the effectiveness of diagnosis and treatment of cancer through support, rehabilitation and palliative care leading to a low rate of cancer morbidity cases in Ghana.^[20]

CONCLUSION

Ghana has consistently recorded a low frequency of kidney cancers since 2014 as a result of implementing its 2012–2016 cancer action plans. The most common type of disease was WT in this study, which occurred mostly in children. RCC was the second-most common kidney cancer in this study, which most occurred among young adults. Other kidney cancers such as sarcoma and urothelial were very uncommon, but occurred more in males than in females. Ghana's campaign towards

achieving good health and well-being through a sustainable development goal has had a great influence on the citizens' participation in activities such as health screening and regular health checkups, and this has aided in the early detection of the disease and lowering the mortality rate.

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Conflicts of interest

There are no conflicts of interest.

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