Epidemiology and Factors Associated with Mortality among Haitian Children and Adolescents Treated for Cancer at a Paediatric Hospital from 2010 to 2014

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ABSTRACT

Background: Paediatric cancers represent about 1% of all diagnosed cancers around the world (1). This study aimed to describe the epidemiology and determine the factors associated with mortality of paediatric cancers managed at a Haitian paediatric hospital.

Methods: This was a cross-sectional study on the cases of paediatric cancers admitted in St Damien Hospital (SDH) in Haiti from 2010 to 2014. The cancers were studied according to the age (0–17 years of age), the gender, the geographic origin, the cancer type, the type of treatment and the therapeutic outcome. The study evaluated whether the gender, an age group, the Department of origin, the type of cancer, the type of treatment, the occurrence of relapse or a complication was significantly associated with mortality among this population.

Results: One hundred and thirty-nine cases of paediatric cancers (77 males, 62 females) were admitted. The prevalence of cancers was 0.76% (95% CI: 0.64%-0.89%). Eleven different types of cancers were diagnosed and the most common ones were the leukaemias (30.93%), renal tumours /Wilms tumour (30.93%), retinoblastoma (15.11%), sarcomas (6.47%) and lymphomas (5.04%). More than 50% of the children with cancer were less than five years of age. The cure rate was 74.1%, the relapse rate 15.10% and the overall mortality rate 25.9%. The odds of dying were significantly higher in children with blood cancers (Odds Ratio (OR) = 2.2; $p = 0.04$), with relapse (OR = 127.5; $p < 0.01$) or a complication (OR = 5.5; $p < 0.01$).

Conclusion: Paediatric cancer care needs to be improved in Haiti, especially for blood cancers, in order to reduce relapse, complications and mortality.

Keywords: Epidemiology, Haiti, mortality, paediatric cancer, risk factors

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INTRODUCTION

Paediatric cancers are rare and represent about 1% of all cancers diagnosed worldwide (1). Several types of childhood cancers have been reported worldwide varying by age, gender, ethnicity and geographic location. Numerous studies have provided important insights in the epidemiology and aetiology of childhood cancers (2, 4, 8). Contrarily to adult cancers that are classified by topography (site) according to the International Classification of Disease for Oncology (ICDO), neoplasms in children are classified by morphology (histology) according to the International Classification of Childhood Cancer [ICCC] (2).

The exact causes of most paediatric cancers are unknown. Oncogenic mutations, lifestyle and environmental factors involved in the development of many adult cancers are probably not responsible of childhood malignancies, as these factors require a long period of time to provoke sufficient DNA damage and trigger oncogenesis (3, 4); Childhood malignancies have however, been associated with constitutional molecular defects found in diseases such as Beckwith-Wiedemann Syndrome and Down Syndrome and hereditary conditions such as Li-Fraumeni Syndrome. They were indeed shown to be involved in the development of embryonic cancers, leukaemias, brain tumours, osteosarcoma and rhabdomyosarcoma (4–6).

The leukaemias and the central nervous system (CNS) tumours are the most common diagnosed cancers among the children around the world (2, 4, 7). According to the North American Association of Central Cancer Registries (NAACCR), the death rates for all childhood and adolescent cancers combined have considerably declined in the last 30 years (1). Cancer is in the United States of America the second cause off all cause-related deaths in children and it is the first cause of disease-related deaths. The diagnosis and management of cancers are an even bigger

burden for the developing countries than for the industrialized countries (7); indeed, the resource-limited countries such as Haiti cannot afford the modern techniques of diagnostics and treatment (8).

Haiti is the only low-income country in the American hemisphere with an overwhelmed medical system. Although childhood cancer is a public health issue around the world, its current status in Haiti is not well known. There are very few physicians trained in the management of paediatric cancers and no national cancer registry is available. This study aimed to evaluate the epidemiology of childhood cancers in Haiti, and to determine the factors associated with mortality among the cases diagnosed and managed at a Haitian paediatric hospital.

SUBJECTS AND METHODS

This was a cross-sectional study on the cases of paediatric cancers admitted and managed in the Oncology Department of St Damien Hospital (SDH), in Port-au-Prince, Haiti, from January 2010 to December 2014. Were included all children and adolescents with a clinical or histologically confirmed diagnosis of malignancy, and were excluded those with a benign tumour. The cases were divided into blood cancers and solid cancers. After obtaining approval of the medical direction of Saint Damien Hospital and the head of the Oncology Department, the medical charts were fully reviewed to collect key data on key variables such as age, gender, the geographic region, the cancer type, the type of treatment and the therapeutic outcome. The number of diagnosed cases, relapse and deaths related to cancer were evaluated for each year of the study period. Statistical analysis was performed using Epi info version 7.1.0. This study evaluated through the calculation of Odds ratios (OR) whether the gender, an age group, the department of origin, the type of

treatment received, the type of cancer (solid tumour *versus* blood tumour), the occurrence of complication or relapse were associated with mortality among this population. Mantel-Haenszel Chi-square test was chosen to determine a significant association of these variables with mortality. A *p*-value of less than 0.05 for any association was considered as statistically significant.

RESULTS

Overall study: The chart review found 139 cases of cancer out of 18 376 admissions during the study period, which gave a cancer prevalence of 0.76% (95% CI: 0.64%–0.89%). Seventy-seven children were males and 62 females (Table 1). The mean age of the population was 5.14 years old, ranging from less than one-year-old to 16 years old. More than 50% of the diagnosed children were less than five years old.

Table 1: Baseline characteristics of the children and adolescents managed for cancer at St Damien Hospital from 2010 to 2014 (n = 139)

VARIABLES	FREQUENCIES	PROPORTIONS (%)	95%CI
Gender	Male (77)	55.4%	46.7% – 63.8%
	Female (62)	44.6%	36.2% – 53.3%
Age	<1 y/o (8)	5.8%	2.5% – 11.0%
	1-4 y/o (66)	47.5%	39% – 56.1%
	5-9 y/o (41)	29.5%	22.1% – 37.9%
	10-17 y/o (24)	17.3%	11.4% – 24.6%

Department of origin	West (99)	71.2%	63.5% – 79.1%
	Artibonite (8)	5.8%	2.5% - 11.1%
	North (6)	4.3%	1.6% - 9.2%
	Southeast (6)	4.3%	1.6% - 9.2%
	Nippes (5)	3.6%	1.2% - 8.3%
	Northwest (5)	3.6%	1.2% - 8.3%
	Center (3)	2.2%	0.5% - 6.2%
	South (3)	2.2%	0.5% - 6.2%
	Grand-Anse (2)	1.4%	0.2% – 5.1%
	Northeast (1)	0.7%	0% - 4%
Type of treatment	**Solid cancers (89):**		
	Chemotherapy only (29)	20.9%	14.4% – 28.2%
	Surgery only (6)	4.3%	1.6% – 9.2%
	Chemotherapy +surgery (35)	25.2%	18.2% – 33.2%
	Chemotherapy + radiation (4)	2.9%	0.8% – 7.2%
	Chemotherapy + surgery + radiation (15)	10.8%	6.2% - 17.2%
	Blood cell cancers (50):		
	Chemotherapy only (43)	30.9%	23.4% – 39.3%
	Chemotherapy + radiation (4)	2.9%	0.8% – 7.2%
	Chemotherapy + surgery (3)	2.2%	0.4% – 6.2%
Relapse	Yes (21)	15.1%	9.6% – 22.7%
	No (118)	84.9%	77.8% – 90.4%
Complications	Yes (68)	48.9%	40.4% – 57.5%
	No (71)	51.1%	42.5% – 59.7%
Death	Yes (36)	25.9%	18.9% – 34.0%
	No (103)	74.1%	66% – 81.2%

y/o; years of age

Types of paediatric cancers: The Figure summarizes the types of paediatric cancers diagnosed during the study period. Solid cancers and blood cancers represent, respectively 64.03% and 35.97% of the diagnosed cancers. The five most common ones were the leukaemias (30.93%), renal tumours /Wilms tumour (30.93%), retinoblastoma (15.10%), sarcomas (6.47%) and lymphomas (5.04%). Renal tumours /Wilms tumour, retinoblastoma and sarcomas were the most common solid cancers diagnosed. Among the blood cancers, acute lymphoblastic leukaemia

(ALL) was the most common finding followed by acute myeloid leukaemia (AML), Hodgkin's lymphoma (HL) and Burkitt's lymphoma (BL).

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Management and outcome: All diagnosed patients have received at least one or a combination of the three types of treatment such as chemotherapy, surgery and radiotherapy. Solid cancers were responsible of 52% of all recorded relapses and 50% of all diagnosed deaths. The overall relapse rate was 15.11%, and it was by far dominated by the leukaemias (38.1%), renal tumours /Wilms tumour (28.6%), retinoblastoma (19%) and lymphomas (10%). Twenty of the 21 cases with relapse died during the study period. Children less than ten years old of age were more affected by death. Thirty-six children died during the study period which gave a mortality rate of 25.9%. It was the highest among patients with leukaemias (44.4%) and renal tumours /Wilms tumour (27.8%). Complications occurred in 48% of all cases; the most common one being infection (27.34%). Among the 36 deceased patients, 28(77.8%) had at least one complication (Figure).

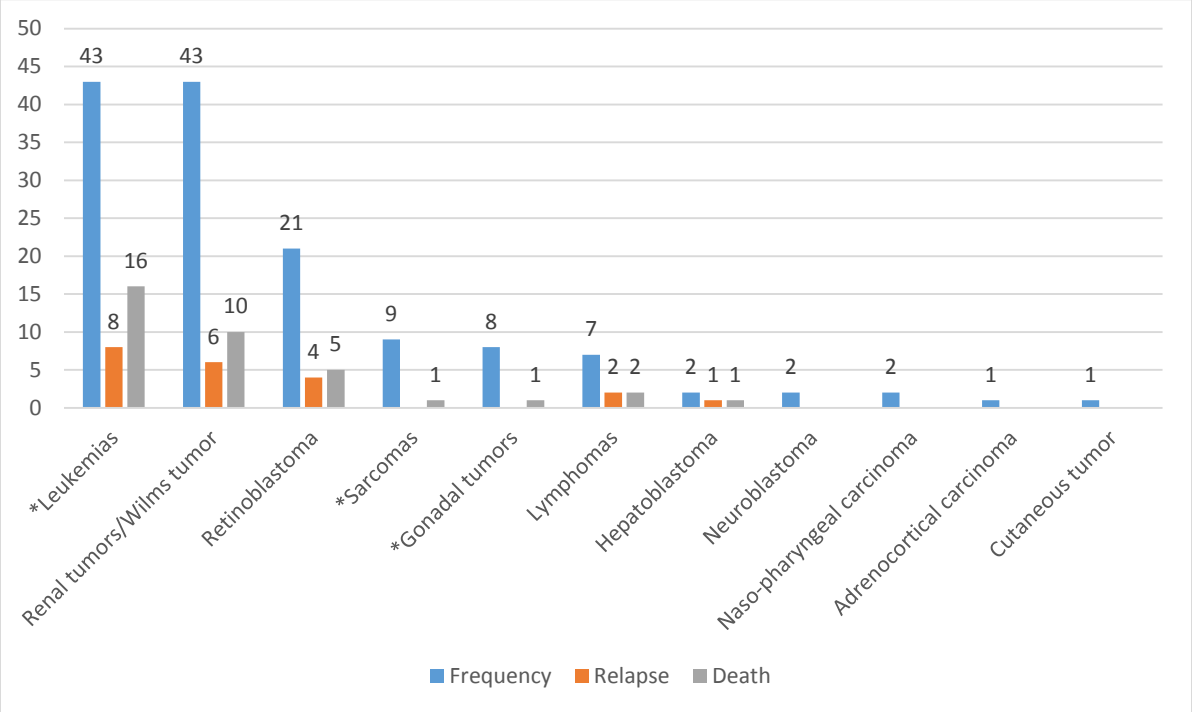

Figure: Frequency, relapse and death per cancer type.

Types of paediatric cancers diagnosed from 2010 and 2014 (n = 139): *Leukemias: Acute lymphoblastic leukaemia (28) + Acute myeloid leukaemia (14) + Chronic myeloid leukaemia (1) = 43 cases; *Sarcomas: rhabdomyosarcoma (7) +osteosarcoma (2) = 9 cases; *Lymphomas: Hodgkin Lymphoma (4) + Burkitt lymphoma (3) = 7 cases; *Gonadal tumours: yolk sac tumour (6) + Germ cell tumour (1) + Ovarian tumour (1) = 8 cases.
Cancer-related deaths in Haitian children and adolescents from 2010 and 2014 (n = 36): *Leukaemias: Acute lymphoblastic leukaemia (7) + Acute myeloid leukaemia (9) = 16; * Lymphomas: Burkitt lymphoma (2); *Sarcomas: osteosarcoma (1); *Gonadal tumours: yolk sac tumour (1)
Relapse cases among Haitian children and adolescents from 2010 to 2014 (n = 21): *Leukaemias: Acute lymphoblastic leukaemia (5) + Acute myeloid leukaemia (3) =8; *Lymphomas: Burkitt lymphoma (2).

Factors associated with mortality. Cancer type, gender, age group, type of treatment, department of origin, occurrence of relapse or complication were evaluated to determine whether they were significantly associated with mortality (Table 2). The odds of dying were significantly higher among children and adolescents with blood cancers compared to those with solid cancers (OR= 2.2; $p = 0.04$); those with the occurrence of any complication (OR= 5.5; $p < 0.01$), and those who relapsed (OR= 127.5; $p < 0.01$). Male children although predominant were not significantly more affected by death than female ones (OR= 1.15; $p = 0.71$).

Table 1: Factors associated with mortality among the children and adolescents managed for cancers at St Damien Hospital from 2010 to 2014.

Predictor variables	**n**	**Odds ratio (OR)**	**OR 95 % CI**	***p*-value**
Gender (female *vs* male)	139	1.15	0.54-2.47	0.71
Age (< 5 y/o *vs* ≥ 5 y/o)	139	1.80	0.83-3.94	0.14
Department of origin (West *vs* the others)	138	0.72	0.32-1.64	0.43
Type of cancer (blood cancers *vs* solid cancers)	139	2.22	1.02-4.82	0.04
Type of treatment for solid cancers (combined *vs* non-combined)	89	2.00	0.72-5.57	0.18
Type of treatment for blood cell cancers	50	1.34	0.23-7.75	0.75
Relapse (Yes *vs* No)	139	127.5	15.99-2016.90	< 0.01
Complications (Yes *vs* No)	139	5.51	2.29-13.29	< 0.01

y/o; years of age

DISCUSSION

This study included a total of 139 cases of paediatric cancers. The age group at diagnosis and the male predominance corroborated to the results reported by other studies (4, 7, 14). According to the literature, paediatric cancers were more prevalent in male patients in almost all types of cancer; however, there was no scientific explanation on the cause of male predominance in childhood cancers (15).The prevalence of paediatric cancers during the study period was below 1%. This prevalence was however, hospital-based and thus, did not reflect the cancer burden among children and adolescents in Haiti. There was nonetheless a possible lack of referral or under-

diagnosis of cancer cases because of the poor availability and accessibility to cancer care. It was highly probable that children and adolescents with acute symptoms seen for example in acute leukaemia could have died before seeking healthcare. Those with symptoms seen in lymphomas could have been misdiagnosed for tuberculosis, which is endemic in Haiti. Children with masses could have had surgery without pathological analysis and could have died of recurrence or during intervention. Moreover, SDH is localized in the capital and thus cannot cover cancer care for the whole country. The absence of cancer specialists in the other departments makes the referrals problematic, especially for the patients living in the countryside or cities far from the capital.

In our study, children less than nine years old were the most affected which was in accordance with the literature reporting that the incidence rates were higher in younger children aged under this age (15). The cause of predominance of cancer in the youngest children is not well known; however, some gene defects, hereditary conditions, exposure to infectious agents and radiation have been highly hypothesized in the development of cancers in children at an early age (4–6, 15). Although likely, it was impossible to determine whether patients less than 15 years old were more affected than older children as it is proven in some studies (13, 15) because the latter are barely admitted or managed in the oncologic department of St Damien Hospital.

Haematological malignancies and CNS tumours are the most prevalent cancers among children worldwide (2, 7, 9, 15). This was not the case in our study for the CNS tumours since the suspected cases seen in SDH were mostly referred to another hospital for surgery or work-up. The absence of radiation therapy in Haiti is a major barrier to the optimal management of CNS tumours.

Racial and ethnic disparities persist in both incidence and outcome of blood cancers. According to the literature, blood cancers particularly ALL were more prevalent among the white

children and are less likely to develop among the black ones (16–19). Haiti has a predominantly black population. Also, as mentioned before, there was a likely under-diagnosis of blood cancers due to a lack of diagnostic techniques and poor access to healthcare.

Although renal tumours /Wilms tumour were among the most prevalent cancers in our study, it was not listed in the top three cancers diagnosed in children particularly in other Caribbean countries (17). Previous studies suggested that race, more than geography or nationality, was a greater risk factor for the development of Wilms tumour and black children appeared to be more susceptible than white ones to develop Wilms tumour (20, 21). Despite of the probability of an under-diagnosis of blood cancers in Haiti, the predominance of renal tumours /Wilms tumour could be due to a possible existence of some gene mutations among the Haitian population. However, in Haiti genetic studies are far from being performed to confirm this hypothesis.

The significant factors associated with mortality related to paediatric cancers in our study were the occurrence of blood cancers, relapse and complication. These findings were most likely related to a delay in the diagnosis of cancers due to late presentation, and a lack of material and human resources at SDH. Also, poor adherence to treatment could negatively influence cancer treatment outcomes and could be detrimental for the treatment of childhood blood cancers which requires prolonged, daily oral or periodic parenteral administration of antimetabolites for up to two years in the maintenance phase (8, 16). This could increase the occurrence of relapse and complication, thus, increase the risk of mortality. Even though African Americans are less likely to develop blood cancers (particularly ALL), numerous studies revealed that when compared with white children they fare worse with therapy than other ethnic groups (16–18). Infection, the most common complication is most likely due to neutropenia related to the use of cytotoxic drugs, well

known for this adverse event and the state of immune suppression that characterizes neoplasms, possibly worsened by a poor nutrition status.

Although the aims of the study were reached, there were some unavoidable limitations. This study was unable to assess the importance of CNS tumours which are with ALL the two most common cancers diagnosed in children worldwide. Also, the absence of molecular biology and cytogenetic testing in Haiti limited this study from establishing some key factors associated with prognosis, particularly in leukaemias, Wilms tumour, retinoblastoma and lymphomas. The results of this study were exclusively based on data collected in the only paediatric oncologic hospital serving mainly one of the ten departments of Haiti; thus, the study population was not representative of the real cancer burden in Haiti's paediatric population and therefore, the results are not generalizable.

CONCLUSION

This study evaluated the clinical epidemiology of cancer among children and adolescents in Haiti; identified the variables associated with the negative outcome of those children managed at SDH for cancer. The predominance of renal tumours /Wilms tumour are of interest and should be followed closely to determine whether this pattern persists in Haitian children living with cancer countrywide. Although the early diagnosis and treatment are important for the management of cancers especially in children, the social and economic situation in Haiti is an immense factor that could delay the diagnosis and the initiation of treatment. The lack of human and material resources hinders the capacity to manage cancers properly in Haiti and could be one of the causes of poor outcome. Nonetheless, the results of this study proved that rigorous actions should be taken to

improve availability and accessibility of paediatric cancer care in Haiti to reduce relapse, complications and overall mortality.

AUTHORS' NOTE

JG Lucien and JJ Bernard worked together to conceive this study. We both participated in its design and the interpretation of the results.

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