

Childhood Cancers in a Tertiary Centre, Southern Nigeria: Spectrum and Outcome of Treatment

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Authors' contributions

This work was carried out in collaboration among all authors. Author GKE designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors NU and NAA managed the analyses of the study. Authors GKE and NU managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Introduction: Though childhood cancers are often amenable to cure even with simple and safe protocols, survival rate is still very low in many low- and middle-income countries where nearly 80% of children with cancer reside.

Objective: To ascertain the pattern and outcome of treatment of childhood cancers in a tertiary centre in southern Nigeria.

Methodology: All cases of childhood cancer admitted into the Paediatric Oncology unit of the University of Port Harcourt Teaching Hospital from January 2011 to November 2019 were reviewed. Their demographics, diagnosis, treatment modalities and outcomes were analyzed using SPSS version 25.0.

Results: A total of 266 cases were analysed: 151(56.8%) males and 115(43.2%) females, with M:F ratio of 1.3:1, aged 1 month to 14 years. Majority (44.7%) were in the 1-4 years age bracket. The majority of children who presented more than 20 weeks after onset of symptoms had retinoblastoma. The most common cancers were acute leukaemias (23%), nephroblastoma (22.1%) and rhabdomyosarcoma (11.6%). Many subjects abandoned treatment (44.4%), and mortality was recorded in 45.1% of the study population.

Conclusion: The distribution of the childhood cancers in this study is similar with report of the

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population based Port Harcourt Cancer Registry, with acute leukaemias, nephroblastoma and rhabdomyosarcoma as most common malignancies encountered. Rates of abandonment of treatment and mortality were high.

Keywords: Childhood cancer; spectrum; outcome; Southern Nigeria.

1. INTRODUCTION

The burden of cancer is increasing worldwide, and children are no exception in this regard. It has been estimated that every 3 minutes somewhere in the world, a family hears the devastating words that their child has been diagnosed with cancer [1]. There has also been marked progress in therapy and supportive care for children and adolescents with cancer in last decades that today, the 5-year net survival rate is approximating 80% in many high-income countries [2,3,4]. The narrative is unfortunately different for low- and middle-income countries (LMICs) where nearly 90% of children with cancer reside, and the scarce available data suggest worse survival estimates, below 20% in most cases, even though childhood cancers are often amenable to cure even with simple and safe protocols [1,2,5,6].

In Sub-Saharan Africa, cancer is characterized by late presentation, low access to treatment, and poor treatment outcomes, while delays in access to cancer treatment result in 80-90% of cases that are in an advanced stage at the time of arrival for treatment [7,8]. The spectrum of childhood cancers, defined as those occurring below the age of 15 years, is also different from those reported in developed countries [9]. Data from 18 Sub-Saharan African countries revealed that the proportion of childhood cancer out of all cancers ranged between 1.4% in Ghana to 10.0% in Rwanda [9]. Beside, in a population based cancer registry in Port Harcourt, Nigeria, children and young adolescents aged 0-19 years constituted 3.7% of cases of cancers [10].

Though a global public health problem, childhood cancers in Nigeria are yet to be recognised as important causes of morbidity and mortality in Nigerian children, whereas much attention is given to adult-type cancers, i.e. breast, cervix, prostate, liver and colorectal, leaving children out of the country's cancer control initiatives [7,11-14]. Furthermore, there is no population-based pediatric oncology tumour registry whereas childhood malignancies differ markedly from adult cancers in their nature, distribution and prognosis [15].

The pattern and outcome of childhood cancers have been reported in various parts of the country, and showed variations in incidences in different geographical locations, though most of the studies were hospital based, and thus may not be a true representation of what is obtained in the communities [11,14,16-18]. Understanding the incidence distribution of pediatric cancers and its changes over time becomes essential for better planning of public health programs, including preventive and therapeutic interventions. Thus this study was conducted to ascertain the pattern and trend in outcome of childhood cancers in a tertiary centre in southern Nigeria.

2. MATERIALS AND METHODS

This was a retrospective survey of children with cancer who were admitted into the Paediatric Oncology unit of the University of Port Harcourt Teaching Hospital (UPTH), Nigeria from January 2011 to November 2019.

The UPTH is one of two tertiary health institutions located in Port Harcourt, the capital of Rivers State, which has a 2016-projected population of 7,303,924 (41% of which are below the age of 15 years) [19]. It is an 800-bed hospital and serves as a general/referral centre for patients within the state and from neighbouring states.

Patients were identified from nurses' records and data on each patient collected from hospital notes. Data on age at diagnosis, gender, duration of illness prior to presentation, diagnosis, treatment modalities and outcome were collected from their case records. Cases with insufficient data were excluded from the study.

Diagnosis was based on histology, cytology, bone marrow studies in the case of haematological malignancies. In some cases, immuno-histochemical markers were employed in the process of diagnosis. Ancillary investigations which also aided in diagnosis included ultrasonography scans, radiographs, computed tomography scan and magnetic

resonance imaging studies. Radiation therapy is not available in our State, thus only patients who could afford travelling out were able to access the facility.

Outcome of treatment was categorised as: (1) completed therapy, (2) still undergoing active treatment, (3) abandoned treatment (defined by missed therapy for 4 or more consecutive weeks, and those who refused therapy), (4) referred to other centres, and (5) death from any cause [20].

Data was entered into a Microsoft Excel Spread Sheet and analyzed using SPSS version 25.0. Chi-Square test was used to test for significance. Statistical significance was set at $P < 0.05$. Results were presented using tables and charts.

3. RESULTS

3.1 Characteristics of Children with Cancer at the UPTH

A total of 266 cases of childhood cancers were analysed, comprising of 151 (56.8%) males and 115 (43.2%) females, with a male to female ratio of 1.3:1. Their ages ranged from 1 month to 14 years, with a mean age of 5.7 years ($SD \pm 4.0$). Under-fives constituted half of the study population, but the predominant age group was 1-4 years (44.7%), followed by 5-9 years (28.2%) (Table 1).

3.2 Duration of Illness in Children with Cancer

The duration of illness prior to presentation ranged from 2 weeks to 144 weeks (36months). Majority of subjects who presented within 4 weeks of onset of symptoms had acute leukaemias, while majority of those who presented more than 20 weeks after onset of symptoms had retinoblastoma (Fig. 1).

3.3 Frequency Distribution of Types of Childhood Cancers

Leukaemias were the most common types of cancers ($n=63$; 23.7%), 81% of them were acute lymphoblastic leukaemia (ALL); followed by renal tumours ($n=60$; 22.6%) with nephroblastoma accounting for 98% of them; soft tissue sarcomas ($n=39$; 14.7%), most of which were rhabdomyosarcoma (79.4%); and lymphomas ($n=30$; 11.1%), most of which were non-Hodgkin lymphoma (NHL) (70%) while Burkitt lymphoma accounted for 20% of the lymphomas (Table 2).

3.3.1 Frequency distribution of cancers in children studied per age group

The five most common malignancies (Table 3) accounted for 74.4% ($n=198$) of all childhood cancers seen during the period under review. Acute leukaemias and NHL were prevalent in the 5-9 age bracket while nephroblastoma, rhabdomyosarcoma, retinoblastoma and neuroblastoma were commonly found among children of 1-4 age group. All children with retinoblastoma were under five years of age.

3.3.2 Modalities of treatment for childhood cancers

All children received supportive care in form of blood/blood product transfusions, antibiotics, analgesics and nutritional rehabilitation. In addition, half of the study population ($n=137$; 51.5%) received only chemotherapy as specific therapy, whereas 36.5% ($n=97$) of subjects received traditional/ herbal medicine or treatment in churches prior to presentation. Sixty-four subjects (24%) received only supportive care as they either died before commencement of specific therapy or abandoned treatment. Only 3.6% ($n=10$) of children benefitted from radiotherapy, which is not available in our State (Fig. 2).

Table 1. Age and gender distribution of children with cancer at the UPTH

Age group of children	Sex				Total	
	Male		Female		Children	%
	Children	%	Children	%		
0 - 11 months	9	3.4	6	2.2	15	5.6
1 - 4 years	70	26.3	49	18.4	119	44.7
5 - 9 years	43	16.2	32	12	75	28.2
10 - 14 years	29	10.9	28	10.6	57	21.5
Total	151	56.8	115	43.2	266	100

Table 2. Frequency distribution of type of childhood cancers

Type of childhood cancers		Children		Total	
		Children	%	Children	%
Leukaemia	Acute lymphoblastic leukaemia	51	81	63	23.7
	Acute myeloid leukaemia	10	16		
	Chronic myelogenous leukaemia	2	3		
Renal tumours	Nephroblastoma	59	98	60	22.6
	Renal cell carcinoma	1	2		
Soft tissue sarcomas	Rhabdomyosarcoma	31	79.4	39	14.7
	Undifferentiated pleomorphic sarcoma	2	5.1		
	Desmoplastic round cell tumours	2	5.1		
	Malignant peripheral nerve sheath sarcoma	1	2.6		
	Angiosarcoma	1	2.6		
	Fibrosarcoma	1	2.6		
	Primitive neuroendodermal tumour	1	2.6		
Lymphoma	Non-Hodgkin lymphoma	21	70	30	11.3
	Burkitt lymphoma	6	20		
	Hodgkin lymphoma	3	10		
Retinoblastoma	Retinoblastoma	26	100	26	9.8
Neuroblastoma	Neuroblastoma	12	-	12	4.5
Germ cell tumours	Yolk sac tumour	5	50	10	3.7
	Malignant teratoma	3	30		
	Dysgerminoma	1	10		
	Testicular mixed germ cell tumour	1	10		
Hepatic tumours	Hepatoblastoma	9	90	10	3.7
	Primary liver cell carcinoma	1	10		
CNS tumours	Brain tumours	6	-	6	2.3
Malignant bone tumours	Osteosarcoma	4	-	4	1.5
Other malignant epithelial neoplasms	Nasopharyngeal carcinoma	3	-	3	1.1
Others	Thymoma, Adenocarcinoma colon, Malignant mesenchymal tumour	3	-	3	1.1
Total		266			100

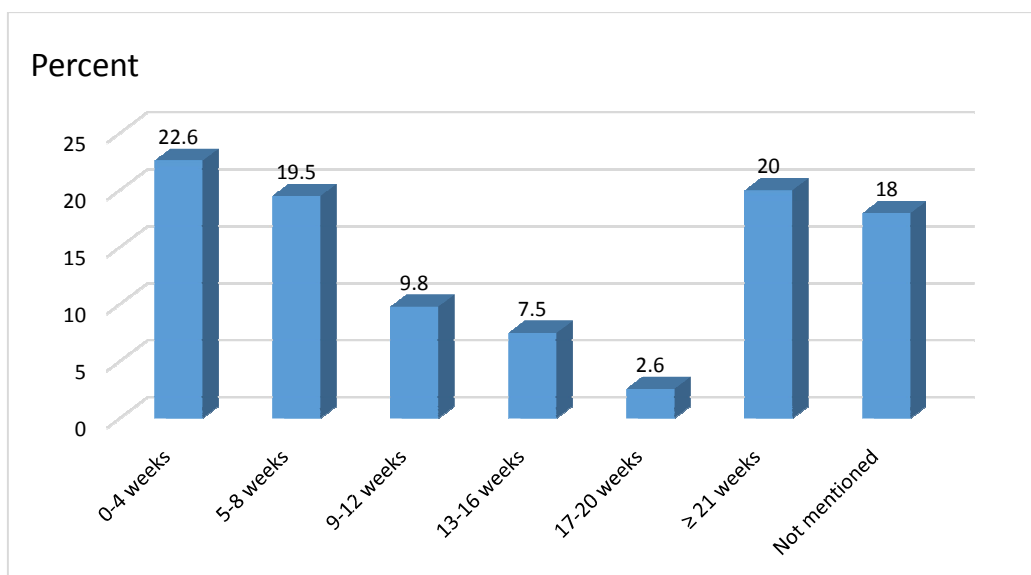


Fig. 1. Duration of illness prior to presentation in children with cancer

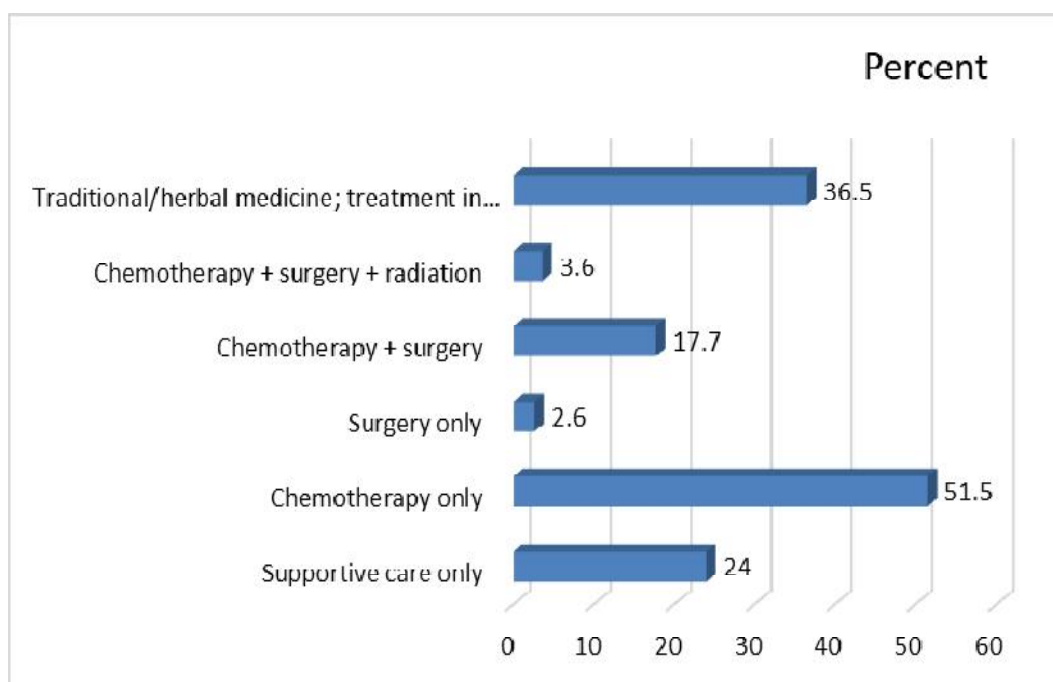


Fig. 2. Modalities of treatment for childhood cancers at the UPTH

3.3.3 Outcomes of treatment for most common childhood cancers

Among children who completed their cancer therapy ($n=19$; 7%), 4 relapsed at 3 months, 2 years, and 3 years later for 2 children. Two of those who relapsed after treatment completion are still undergoing therapy while the other 2 died

in the course of treatment. Many subjects ($n=120$; 44.4%) defaulted with or without commencement of specific treatment, and 45.1% died, while the 3 most common cancers accounted for two-third ($n=71$; 59.1%) of the mortalities (Table 4). However, there was no significant differences between variables ($P=0.1004$).

Table 3. Frequency distribution of cancers in children studied per age group

Type of cancers	0-11 months		1-4 years		5-9 years		10-14 years		Total (n=266)	
	Children	%	Children	%	Children	%	Children	%	Children	%
Acute Leukaemias	1	1.6	18	29.6	26	42.6	16	26.2	61	23
Nephroblastoma	5	8.5	35	59.3	13	22	6	10.2	59	22.1
Rhabdomyosarcoma	1	3.2	16	51.6	8	25.8	6	19.4	31	11.6
Retinoblastoma	3	11.5	23	88.5	0	0	0	0	26	9.8
Non-Hodgkin lymphoma	0	0	4	19	9	42.9	8	38.1	21	7.9
Neuroblastoma	0	0	9	75	2	16.7	1	8.3	12	4.5

Table 4. Outcome of treatment for most common childhood cancers

Most common cancers	Outcome of treatment				
	Completed therapy	Still on treatment	Referred	Abandoned treatment	Died
Acute Leukaemias	2	2	0	20	38
Nephroblastoma	5	2	3	28	22
Rhabdomyosarcoma	1	3	0	17	11
Retinoblastoma	2	0	0	13	11
NHL*	1	0	1	9	10
Neuroblastoma	0	0	0	4	8
Others	7	3	4	27	20
Total: n=266 (%)	18 (6.7)	10 (3.8)	8 (3)	118(44.4)	120 (45.1)

* NHL: Non-Hodgkin lymphoma; P=0.1004

4. DISCUSSION

This study showed male predominance among children with cancer, which was comparable with previous reports in other centres within Nigeria and in other resource-limited countries [10,11,14,16,21]. The reason for this preponderance is not certain, however, it is in agreement with global trends [22]. In this series the predominant age group was 1-5 years, which is similar to previous reports, and could be related to the high frequency of embryonal tumours in that age bracket [11,14]. But, it is at variance with report of a study in Uyo where the predominant age group of children with cancer was 5-9 years, which could be due to the type of cancers prevalent in the region [16]. Besides, that study included children up to 17 years of age and the median age at diagnosis of cancers was 8 years [16].

In this study, the five most common types of cancers were acute leukaemias (23%), nephroblastoma (22.1%), rhabdomyosarcoma (11.6%), retinoblastoma (9.8%), and non-Hodgkin lymphoma (7.9%). They represented 74.4% (n=198) of all cancers seen, and this is consistent with report of the population based Port Harcourt Cancer Registry, even with its lower sample size of children [10]. This constancy is important because it reflect the profile of childhood cancers in Rivers State, which can be leveraged upon to advocate for preventive and therapeutic intervention programmes at the state level.

Nephroblastoma, one of the commonest cancers among African children, was the most occurring solid malignancy in this study and second in the Uyo series [9,16]. In a previous series in this same centre, it was the most prevalent cancer (26.7%), though the study had a smaller sample size [23].

The findings in this study differ from those of a report in Zaria where retinoblastoma had the highest frequency of childhood cancers (34.5%), which was attributed among others, to the presence of Radiation therapy facilities in that institution, one of the main radiotherapy centres in the North West geopolitical zone, followed by Burkitt lymphoma (15.7%) and leukaemia (12.2%) [11]. On the other hand, Burkitt lymphoma (26.2%) was the most prevalent cancer among children in the Uyo study, followed by nephroblastoma (14.3%), and was 3rd most frequent cancer (13.2%), after

retinoblastoma (26.4%) and rhabdomyosarcoma (14.3%) in a study in Ibadan [16,24]. Though said to be the most common childhood malignant tumour in Nigeria, Burkitt lymphoma was not common in the present study as well as in the afore mentioned Lagos series as it represented 2.2% and 1.1% of cancers seen respectively [14,25]. The decline in the frequency of Burkitt lymphoma in some centres within Nigeria has been reported, and has been attributed to improvement in living conditions and better malaria control measures, given the role of malaria in endemic Burkitt lymphoma [14,25].

What was found in this series was also at variance with report of the Yemen series, where the most common group of malignancies were haematological malignancies (47% of cases), followed by central nervous system malignancies (15%), which is similar to the pattern of childhood malignancies in most parts of the developed world [3,26,27]. However, the paucity of Central Nervous System tumours in this series has been previously reported in this same centre and in several series in Nigeria, except in Ibadan where it accounted for 9.9% of childhood cancers over a 2-year review period [11,14,16,17,24]. It is possible that most suspected cases of brain tumours are referred to that centre because of availability of facilities for management of such cancers. The variance in ranking of common cancers may highlight the need to tailor cancer control and prevention programmes to specific local needs.

The treatment of childhood cancer has remained challenging in Nigeria. In this study, the commonest modality of specific treatment of childhood cancer was chemotherapy, while less than 5% of subjects benefited from radiation therapy. Similar findings have been previously reported [11,16]. It is noteworthy that even in the Zaria series, only 1.2% of subjects had radiation therapy which is available in that centre, and that was attributed to financial constraints and non-availability of pediatric focused radiation facilities [11]. A third of the study population patronised traditional/herbal medicine practitioners and/or churches before presenting to the hospital. Though common in the country, this practice is worrisome as can be associated with late presentation which can compromise treatment outcome [16,24].

Childhood cancer is a relatively rare disease but highly curable and cost-effective [9].

Besides, the two most common cancers in this study, acute leukaemia and nephroblastoma which together accounted for 45% of malignancies seen, are known to have good prognosis in developed countries with cure rates above 85% [3]. However, a low rate of completion of therapy (6.7%), high rate of abandonment of therapy (44.4%) as well as high mortality (45.1%) were found in this study. This worrisome trend has been reported in this centre previously and in various parts of Nigeria [11,14,16,17]. It is possible that children who abandon treatment would patronise alternate sources of healthcare for solution [14,16,24]. Further studies are needed to understand the underlying reasons for abandonment of treatment, ascertain the fate of those children, and proffer solutions to reduce suffering for both the child and family so as to improve treatment adherence.

The poor outcome of childhood cancers had been attributed to several factors which, though not explored in this study, were similar in many reports and included among others late presentation, financial constraint as its financing is mainly through out of pocket expenditure, inability to access appropriate treatment, but also inadequacies of health systems [11,14,16,24,28]. This show that urgent attention should be given to childhood cancers to improve patients' care and outcome.

Notwithstanding, it has been showed that access to early diagnosis when symptomatic, coupled with early intervention are the main factors influencing outcome for childhood malignancies, as it is generally not possible to prevent cancer in children [5,29]. Besides, early diagnosis is relevant in all settings and improves survival for many cancers [5,24]. Childhood cancers are known to be associated with a range of warning symptoms that can be detected by families and by trained primary health care providers [5]. Thus, it becomes important that childhood cancer awareness programmes be included in advocacy and social mobilization activities, as one of the important ways of reducing the burden of cancer in children [7,30].

Limitations: Being a retrospective one, our study has various limitations, including exclusion of many cases because of insufficient data and inability to explore factors that influenced poor outcome.

5. CONCLUSION

The distribution of the childhood cancers in this study is similar with report of the population based Port Harcourt Cancer Registry, but different from reports of other centres in Nigeria. Acute leukaemias, nephroblastoma and rhabdomyosarcoma were the most common malignancies encountered, with low rate of completion of therapy, high default and high mortality rates.

Advocacy/awareness campaigns at all levels of healthcare for early detection and prompt treatment, couple with free treatment for all childhood cancers and social support to ensure completion of therapy and improve outcome are recommended, alongside the provision of pediatric-focused radiation facilities in hospitals that handle many cases of childhood cancer.

CONSENT

It is not applicable.

ETHICAL APPROVAL

Approval for the study was obtained from the hospital's medical Ethics Committee.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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