

Pediatric malignancies in Kano, Northern Nigeria

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Background: With effective immunization control of several devastating childhood infections in the developing world, non-infectious diseases such as malignancies have become increasingly important causes of pediatric morbidity and mortality. Therefore this 10-year retrospective study was undertaken to evaluate and document the pattern of childhood cancers in our locality.

Methods: We reviewed 438 childhood (≤ 15 years) malignancies diagnosed at the histopathology and hematology laboratories of our teaching hospital in a 10-year period (2001-2010).

Results: The 438 malignancies comprised 10.9% of all cancers. The malignancies frequently seen in early childhood (0-4 years) accounted for 46.1% and in late childhood (5-9 years) for 34.7%. Retinoblastoma (30.6%), Burkitt lymphoma (19.9%) and acute leukemia (16.9%) were the most common pediatric cancers. Unlike in most other parts of the world, acute myeloid leukemia was slightly more prevalent than acute lymphoblastic leukemia.

Conclusions: Although there were notable differences, our findings were in broad agreement with those of most other sub-Saharan African series, but differed markedly from those in the Western world and other high income countries. Further studies are required to identify the environmental factors for the high prevalence of non-familial retinoblastoma and possibly acute myeloid leukemia.

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Introduction

With effective immunization programs successfully combating previously common devastating childhood infections in the developing world, the relative burden of non-infectious childhood diseases such as cancer has increased. Consequently, pediatric cancer has become an increasingly important cause of childhood morbidity/mortality and a major public health concern.

In view of the higher birth rates and younger population in the developing countries, childhood malignancies are accordingly more prevalent than in the developed world. Childhood cancers comprise just 0.5%-2% of malignancies in the industrialized countries,^[1-3] but 4.3%-12.5% in the developing countries.^[4-8] Not surprisingly, over 80% of the global childhood cancers are estimated to occur in the developing countries.^[9,10]

In the low income developing countries (LICs), pediatric cancer survival is low, largely because of the poor access to good quality pediatric oncology care. Since many of the LICs lack proper population-based cancer registries, there is a dearth of epidemiologic data on common childhood malignancies. Such data are essential for optimal channeling of scarce healthcare resources in the LICs.^[10,11]

The need for up-to-date cancer data is particularly crucial in view of the striking ethnic and regional variations that have been documented, sometimes even within a country.^[12] In Nigeria, for instance, retinoblastoma is the commonest childhood cancer in Lagos, while in neighboring Ife about an hour and half drive away, Burkitt lymphoma is the premier pediatric malignancy.^[13,14] It is therefore imperative to evaluate and properly document the pattern of childhood cancer in our locality here in Kano, Northern Nigeria as existing studies from other parts of the country may not reflect our situation.

Methods

This is a 10-year (2001-2010) retrospective review of all childhood (0-15 years old) malignancies diagnosed at the pathology and hematology laboratories of Aminu Kano Teaching Hospital (AKTH) in Kano,

Northern Nigeria. AKTH is the major tertiary health institution offering histo/cytopathology and specialized hematology services to Kano and the neighboring states of Jigawa, Katsina and Bauchi.

All histopathology sections were formalin fixed, paraffin embedded, and then stained with hematoxylin and eosin. Special stains were deployed where necessary, but immunohistochemistry was not employed as this technique has only recently become available in our laboratory. Fine needle aspiration cytology slides, which were the main diagnostic modality for Burkitt lymphoma, were stained with papanicolau and Diff-Quick.

For hematological malignancies, air dried blood/bone marrow smears were fixed in methanol and stained with Romanowsky stains (Leishman or May-Grumwald Giemsa). Ancillary molecular diagnostic techniques like flow cytometry, cytogenetics and immunocytochemistry were not employed as they are not available in our hematology laboratory.

Histopathology and hematology slides were then examined and reported by consultant pathologists and hematologists. Data (age, sex, diagnosis, etc) were collected from laboratory records and the hospital cancer registry. Data from cancer patients were categorized in accordance with International Classification of Diseases – Oncology (ICD-O) guidelines and WHO recommended pediatric age groups.

Results

A total of 438 childhood malignancies were diagnosed during the 10-year study period, which comprised 42% of all pediatric neoplasms and 10.9% of all cancers.

Pediatric cancers were most commonly seen in early childhood (1-4 years) and late childhood (5-9 years), accounting for 43.2% and 34.7% respectively (Table). Malignant tumors were relatively less prevalent among adolescents (10-15 years) and infants (<1 year). Slight male preponderance was observed with a male to female ratio of 1.3:1.

Retinoblastoma, the commonest pediatric cancer, accounted for almost one-third (30.6%) of all childhood malignancies. The overwhelming majority (91%) of these ocular tumors occurred within the first five years of life. Burkitt's lymphoma, the second most frequently encountered pediatric malignancy, comprised one-fifth of the malignancies. This lymphoid malignancy was mainly seen in late childhood (5-9 years), and jaws were the commonest site.

Leukemias as the 3rd commonest pediatric cancer accounted for 16.9% of all childhood malignancies. Acute myeloid leukemia (AML) was slightly more prevalent (37 cases) than acute lymphoblastic leukemia (ALL) (34 cases), while juvenile chronic myeloid leukemia and malignant histiocytosis made up the remaining 3 hemtological malignancies. Leukemia mostly afflicted the 1-10 year age group, particularly the late childhood group (5-9 years).

Other (non-retinoblastoma) malignant embryonal tumors (nephroblastoma, neuroblastoma, rhabdomyosarcoma) were the 4th largest category, collectively comprising 15.2%. Significantly, there were no brain tumors in this study.

Collectively, hemato-lymphoid malignancies (leukemias, lymphomas) were the most prevalent, followed by embryonal cancers, namely retinoblastoma, nephroblastoma, neuroblastoma and embryonal rhabdomyosarcoma.

Table. Pediatric malignancies in Kano, Northern Nigeria

ICD-10	Tumor	Number of cases	Percentage	Male	Female	<1 y	1-4 y	5-9 y	10-15 y
C69.2	Retinoblastoma	134	30.6	71	63	8	114	12	-
C83.7	Burkitt's lymphoma	87	19.9	48	39	-	14	52	21
C91-92	Leukemia	74	16.9	48	26	2	19	33	16
C49.M50	Rhabdomyosarcoma	29	6.6	13	16	-	10	11	8
C64	Nephroblastoma	26	5.9	17	9	2	16	8	-
C83-89	Other non-Hodgkin lymphoma	22	5.0	13	9	-	2	13	7
C81	Hodgkin lymphoma	18	4.1	12	6	-	2	7	9
C74.9	Neuroblastoma	12	2.7	7	5	-	9	3	-
C62	Malignant ovarian tumors	11	2.5	-	11	-	-	4	7
C46	Kaposi sarcoma	5	1.1	2	3	-	1	2	2
C62	Malignant testicular tumors	3	0.7	3	-	-	1	2	-
C44	Skin cancer	3	0.7	1	2	-	-	1	2
C40	Malignant bone tumors	4	0.9	3	1	-	-	2	2
C49	Other sarcomas	10	2.3	6	4	1	1	2	6
	Total	438	100.0	244	194	13	189	152	80

Discussion

The 438 pediatric malignancies in this review accounted for 10.9% of all cancers during the study period, which is much higher than the 0.5%-2% documented in the developed countries^[1-3] but consistent with studies in other parts of Africa: 11.5% in Tanzania^[6] and 12.4% in Ibadan, Nigeria.^[7] This disparity between Africa and the developed world can be largely explained by demographics as developing countries like Nigeria have higher birth rates and consequently larger proportion of children/young people in their population.

Slight male preponderance (M:F=1.3:1) was observed in this review, which is comparable to other studies in Nigeria and around the world varying from 1.2:1 to 1.5:1.^[8,13-19] The peak age incidence of pediatric malignancies in Kano was 46.1% in early childhood (1-4 years), followed by 34.7% in late childhood (5-9 years). Retinoblastoma which was the commonest childhood cancer in this review largely accounted for the prominent early childhood peak, as the overwhelming majority (91%) of cases of this ocular malignancy occurred within the first 4 years of life.

An early childhood pediatric cancer peak is also seen in the resource-rich high income countries (HICs) but is largely due to acute leukemia which is the most frequent childhood malignancy.^[20,21] In most of other sub-Saharan African studies where Burkitt lymphoma was the leading childhood cancer, the peak age group was in late childhood (5-9 years).^[6,14,16,18,19]

Zaria, a neighboring northern Nigerian city, also documented retinoblastoma as the most frequent childhood cancer.^[17] The relatively high proportion of retinoblastoma in these two northern Nigerian centers (Zaria, Kano) is partly attributable to the fact that the pathology laboratories of both teaching hospitals, where the studies were carried out, also serve major eye specialist referral centers in Kano and Kaduna. High rates of retinoblastoma have also been documented in other African countries with this ophthalmic tumor among the top 3 childhood cancers in Tanzania, Ghana, Kenya, Malawi, Zambia, Congo and other parts of Nigeria.^[6,13,18,19,22-24] Racial predisposition seems unlikely since black children in the USA have the same low rates of retinoblastoma (3%) as white kids,^[25] in contrast to 11.4% to 28% in African series.^[13,14,19,22-24] Globally, non-familial retinoblastoma has been linked to poverty as it is also high in several LICs outside Africa,^[26,27] suggesting some yet to be defined poverty-related environmental carcinogen (possibly infectious).^[27]

Burkitt lymphoma, the second most frequent childhood cancer in Kano, accounted for 20%. As in other published studies of endemic Burkitt lymphoma, the peak age group was late childhood (5-9 years) although male preponderance was less marked, with

a male to female ratio of 1.2:1 in Kano as against the established 2:1.^[28,29] In most parts of southern Nigeria and much of tropical Africa, endemic Burkitt lymphoma as the commonest childhood cancer comprised 20%-52% of pediatric malignancies.^[14,16,19,29,30] In several northern Nigerian studies, however, Burkitt lymphoma was displaced from the top position by other childhood cancers.^[15,17] This relatively lower frequency of Burkitt lymphoma in northern Nigeria is probably due to climatic factors.

Dennis Burkitt, who defined this childhood malignancy, observed that the lymphoma is largely confined to areas with annual rainfall of more than 50.8 cm and temperature consistently above 15.5°C.^[31] These climatic factors favour mosquito transmission of malaria, which is a known risk factor for endemic Burkitt lymphoma. Sahelian northern Nigeria is much dryer than the south region with substantially lower annual rainfall, and during the dry harmattan season, temperatures can drop precipitously to 15.5°C.

The relatively low incidence of Burkitt lymphoma in this review could also be part of a gradual decline documented in parts of southern Nigeria, notably Ibadan and Lagos.^[13,32,33] In Lagos, retinoblastoma has displaced Burkitt lymphoma as the commonest childhood malignancy.^[13,33] Ojesina et al^[32] ascribed the decline to improved living standards and malaria control.

Leukemia (mostly acute leukemia), the 3rd most frequent childhood malignancy in Kano, comprised 16.9%. Though somewhat higher than several other Sub-Saharan African studies,^[15,23,24,34] this figure is much lower than studies among Caucasian populations in both developed and developing countries where acute leukemia is the most frequent pediatric cancer.^[1,4,8,21,22] In the United States, Europe, Middle East and the Indian subcontinent, leukemia comprised a third of childhood cancers.^[1,4,8,20,21]

The lower incidence acute leukemia in Africa and other low income countries has been ascribed to underdiagnosis as the clinical features are somewhat non-specific with no obvious tumor mass as in solid malignancies.^[11] Furthermore, confirmation of leukemia diagnosis requires specialized hematology laboratory with marrow aspirate/biopsy services that are in short supply in resource-poor low income African countries with poor health care coverage.

Consequently, many acute leukemia cases are misdiagnosed as infectious or other non-neoplastic disorders which they can mimic in the early stages. In addition, unlike in several solid malignancies which often permit survival for several months, acute leukemia can be rapidly fatal, thereby obviating late diagnosis.

Although underdiagnosis partly explains the reported low incidence of acute leukemia in black

African series, racial genetics also plays a role as black children in the United States also have markedly lower rates of acute leukemia.^[27,35,36]

Unlike in other high acute leukemia incidence climes where ALL constitutes the overwhelming majority (75%-80%),^[36] AML was slightly more common than ALL in the present study. This is consistent with the relatively high incidence of AML in several other African studies.^[37-40] While it is probable that the lower incidence of ALL among black children accentuates the proportion of AML, a real higher AML incidence due to some racial/environmental predisposition cannot be discounted given the paucity of childhood AML in most other parts of the world.^[36] The high incidence of AML has also been reported among black American children in late childhood.^[36,41,42] This is consistent with the age profile of acute leukemia in Kano, which peaks in 5-9 years in contradistinction to 0-5 years in most ALL-dominated high acute leukemia zones.^[1,8,20,21] Despite this obvious implication of racial genetics in high AML incidence, in-utero or postnatal exposure to several environmental carcinogens (hydrocarbons, alcohol, marijuana, pesticides, ionizing radiation) that have been tenuously linked to AML cannot be ruled out, particularly as high AML incidence has also been reported in some non-Negroid populations in parts of Asia.^[41-43]

Brain tumors, the second most frequent pediatric cancer in the Western countries,^[1,2,10,20] were conspicuously absent in this laboratory based study, because our center has no neurosurgery unit. Consequently, most cases of intracranial tumors are referred to elsewhere after preliminary clinical/radiological diagnosis. However, studies from other parts of Nigeria and the rest of black Africa suggest a low incidence of tumors of the central nervous system.^[6,13-18,22-24]

Although our findings were broadly in agreement with most other sub-Saharan African series, but differed markedly from those from the western countries. Further studies are required to identify the environmental factors for the high incidence of retinoblastoma and possibly AML.

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Contributors: Ochicha O proposed the study and wrote the first draft. All authors contributed to the design and interpretation of the study and to further drafts.

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