

Cancers in young patients in Uyo (Niger-delta region of Nigeria): magnitude of the problem and histopathological prolife

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Abstract

Cancers are thought to be rarer in younger population, but emerging data show an increasing incidence of these diseases. The aim of this study was to evaluate the clinicopathological characteristics of cancer among young patients (≥ 30 years) in Uyo, Nigeria. All specimens were collected and reviewed during the period January 2007-December 2012; complete clinicopathological data were also considered. A total of 108 cases of proven cancers were diagnosed (3.4%), accounting for 14.1% of all malignancies. A male:female ratio of 1:3.2 was recorded. Among 0-14-year-old patients, the most common malignancy was embryonal cancer (50.0%), followed by non-Hodgkin's lymphoma (18.8%). Carcinoma of the breast and soft tissue sarcoma represent first and second cancers in those patients (40.7% and 13.0% respectively). Carcinoma of uterine cervix and nodal lymphomas were the third and fourth most common cancers respectively (10.2% and 7.4%), significantly higher in the 21-30 years and 0-10 years age groups. Invasive ductal carcinoma, squamous cell carcinoma, Kaposi sarcoma and Hodgkin's lymphoma were the most common histologic types of cancers in breast, uterine cervix, lymph node and soft tissue (79.6%, 90.0%, 44.4%, 50.0% respectively). This study shows that embryonal cancer was the most common malignancy in patients aged 0 to 14, while carcinoma of the breast and soft tissue sarcoma were the two most common cancers in patients from 5 to 30 years-old.

Introduction

Cancer is a dreadful disease which brings about tremendous psychological suffering, social distress and hardships to the patients and their relatives.¹ Beside well known childhood cancers, spectrum of cancer types of varying magnitude and fatality have been recorded

among adolescent and young adults (AYA) globally.² Although, cancers among children and adolescents accounted for 1% of all new cancers diagnosed in the United States, prompt identification of risk factors among them and perhaps early treatment will help to stem down the proven mortality and morbidity.³

The incidence of cancer in patients aged 30 years or younger varies from region to region. In USA, the annual incidence rate of cancer in children and adolescents was reported to be 186.6 per 1 million in children aged 0 to 19 years.³ On the other, another study in North America recorded an increased incidence of cancer in AYA with a rise from 346 per million per year for those aged 20 to 24 years to 604 per million per year for those aged 25 to 29 years.⁴ In Queensland, Australia, varying incidences of cancers in relation to age group ranging from 0.6% in childhood (0-14 years) to 2.0% in adolescents and young adults (aged 15-29 years) were reported.⁵ This also compares relatively with findings from a study conducted in England and Wales where annual incidences of cancers ranged from 122 per million children aged less than 15 years to 150-200 per million adolescents aged 15-19.⁶ Findings from another study in UK indicated that the incidence of cancer in adolescents aged 15-19 years old is 50% higher than that in younger persons while rates in both males and females were significantly higher in the persons aged 20-24 years than those aged 15-19 years.⁷

Some studies have proposed that cancers in the younger population exhibit features unique to their age group (15 to 29 years), including a distinct cancer epidemiology, evolving hormonal milieu, maturing development, transitions in autonomy, increasing demands in education, entry into the workplace and family responsibilities.^{4,5} A study has also proposed that AYA have an exponential risk of developing cancer as they advance in age, thus suggesting a basic carcinogenic exposure that is age-dependent including telomerase shortening or a mutation-to-malignancy rate that increases constantly with age.⁸

In addition, it has been agreed that lack of a well structured health insurance for this younger population is associated with delay in diagnosis which is worsened by the fact that most insurance companies in developing countries like ours are not interested in providing insurance coverage for patients with cancers owing to worse outcome and reduced survival rate.^{2,3}

Although clear gender predilection has not been described for all cancers in younger population, certain cancers however are sex-specific. In boys, the risk of testicular germ cell tumors is significantly higher in early childhood, and AYA above 15 years while ovarian

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germ cell tumors occur commonly in post-pubertal girls.⁶ Furthermore, germ cell tumors are markedly more common in males than females in the older age groups while malignant melanoma is more common in females in those aged over 15 years, as are carcinomas of the thyroid, breast and genitourinary tract.⁶ For most sex-specific cancers, there is usual underlying dependence on pro-oncogenic hormones which bind to numerous specific receptors that abound the primary tissues, thus amplifying the process of oncogenesis.⁶

The most common cancers among children, adolescents and AYA vary by age.

Studies conducted in different countries in patients aged 30 years and younger revealed a spectrum of cancer types.⁵⁻¹⁶ This is exemplified by findings from a study conducted in USA where lymphomas, melanoma, testicular cancer, female genital tract malignancies, thyroid cancer, bone and soft tissue sarcomas, leukemia, central nervous system (CNS) cancers, breast cancer, and non-gonadal germ cell tumors were reported to have accounted for 95% of all the cancers in AYA.² Another study in USA corroborating the aforementioned studies showed that acute lymphoblastic leukemia (ALL) (26%), brain and CNS tumors (21%), neuroblastoma (7%), and non Hodgkin's lymphoma (6%) constituted four leading cancers in children while Hodgkin's lymphoma (15%),

thyroid carcinoma (11%), brain and CNS tumor (10%) and testicular germ cell tumor were four most common cancers in adolescents.³ Similarly, findings from studies conducted in North America including USA and Canada are skewed towards preponderance of malignant epithelial tumors (carcinomas) in young adults which is in discordance with preponderance of Hodgkin disease, germ cell tumors, bone and soft tissue sarcomas, acute leukemia, brain tumors, non-Hodgkin lymphoma, melanoma and thyroid carcinoma in adolescents.^{4,17}

In addition, there are many predisposing factors that have been implicated in the aetiopathogenicity of most cancers in childhood and AYA patients while few predisposing factors are cancer-specific. Environmental factors including ionizing radiation exposure and cigarette smoking as well as genetic factors including chromosomal and gene disorders have being implicated in many cancers including cancers of the skin, gastrointestinal, lungs, and breast as well as malignant lymphoma and leukemias.^{4,19}

Available data from many studies have shown that the AYA patients with cancer tend to have worse prognosis compared to childhood and pure adult cancers.^{18,19} This relatively poor prognosis in AYA patients has been proposed to be due to many factors. Apart from racial and ethnic disparities noted for cancers in AYC patients, other attributing factors to this dismal prognosis include lower socioeconomic status, poor parental education, poor health insurance status, untimely diagnosis, non-enrollment in cooperative group clinical

trials, inadequate knowledge about the cancer diagnosis, poor quality of treatment and supportive care, differences in disease biology, genetic polymorphisms in the metabolism of chemotherapeutic drugs, and variations in adherence to therapy.^{3,18,19}

The study is aimed at evaluating the clinicopathological characteristics of cancers among those patients aged 30 years and below in the Department of Histopathology, University of Uyo Teaching Hospital, Uyo, Akwa-Ibom state, Nigeria.

Materials and Methods

A retrospective study was undertaken to review the histopathology reports of all cancers diagnosed in patients aged 30 years or younger at the department of Histopathology of University of Uyo Teaching Hospital, Uyo, Niger-Delta region of Nigeria between January 2007 and December 2012. It is a referral centre for other government and private hospitals in and around the Akwa-Ibom State, South-South Nigeria.

Necessary patients' biodata, clinical and pathological data were retrieved and recorded. Routine Hematoxylin and Eosin (H&E) staining and where necessary histochemical studies were carried out. These data were analyzed in terms of frequency, age, sex distribution, anatomical sites and histologic characteristics of pathologic lesions using Microsoft Excel 2007. The data for these patients were presented in Table 1.

Results

A total of 108 cases of proven cancers were diagnosed in patients aged 30 years or below representing 3.4% of total specimens received during five years under review. This also accounted for 14.1% of all malignancies diagnosed.

The ages ranged from 0.2 to 30 years with a mean age of 23.1 years and a modal age of 30.0 years. Cancers in the younger population peaked in 21-30 years age group (72.2%). A male to female ratio of 1:3.2 was recorded.

Among 0-14 years old patients, the most common cancer was embryonal cancer (50.0%). The next most common cancer was Non-Hodgkin's lymphoma (18.8%), this is followed by soft tissue sarcomas (12.5%). Besides the three leading cancers in patients aged 0-14 years, other cancers were seen. These included teratoma, mucoepidermoid carcinoma and malignant histiocytosis which accounted for 6.3% of cases each.

Carcinoma of the breast and soft tissue sarcoma ranked first and second cancers in patient who were 30 years or younger, predominantly 5-30 years old (40.7% and 13.0%) respectively; and significantly higher in females within the 21-30 years age group in 97.7% and 21.4% of cases respectively. Carcinoma of uterine cervix and nodal lymphomas were the third and fourth most common cancers respectively (10.2% and 7.4%), and significantly higher in the 21-30 years and 0-10 years age groups respectively.

Among AYA, invasive ductal carcinoma,

Table 1. Age and sex distribution of cancers in younger patients.

	0-10		11-20		21-30		Subtotal		Total (%)
	M	F	M	F	M	F	M	F	
Breast	0	0	0	1	0	43	0	44	44 (40.7)
Soft tissue	3	2	4	2	0	3	7	7	14 (13.0)
Cervix		0		0		11	11		11 (10.2)
Lymph node	4	1	1	0	1	1	6	2	8 (7.4)
Ovaries		0		1		5	6		6 (5.6)
Skin	0	0	0	0	4	1	4	1	5 (4.6)
Salivary gland	0	0	1	1	2	0	3	1	4 (3.7)
Nasopharynx	0	0	0	3	0	1	0	4	4 (3.7)
GI/T	0	0	0	0	0	2	0	2	2 (1.8)
Prostate	0	0		2		2			2 (1.8)
Kidney	1	1	0	0	0	0	1	1	2 (1.8)
Endometrium		0		1		1	2		2 (1.8)
Eye	0	0	1	0	1	0	2	0	2 (1.8)
Testis	0	1		0		1			1 (0.9)
Adrenals	0	1	0	0	0	0	0	1	1 (0.9)
Total	8	5	8	9	10	68	26	82	108

squamous cell carcinoma, Kaposi sarcoma and Hodgkin's lymphoma were the most common histologic types of cancers of breast, uterine cervix, lymph node and soft tissue (79.6%, 90.0%, 44.4%, 50.0%) respectively.

The majority (61.4%) of the breast cancer (invasive ductal carcinoma) patients had high grade histologic lesion while only 13.6% of the patients had low grade histologic lesion. The majority (50.0%) of the cervical cancer (squamous cell carcinoma) patients had high grade histologic lesion while only 30.0% of the patients had low grade histologic lesion.

The majority (45.9%) of the breast cancer patients who were 30 years or younger presented in advanced stages of the disease with regional lymphadenopathy (9.1%), ascites (6.8%) and distant metastasis (4.5%).

Discussion

Cancer is a dreadful disease that has no respect for age, sex, racial, ethnic and socio-economic status. It also brings about tremendous psychological suffering, social distress and untold hardships to the patients and their relatives.¹ Available literature have clearly defined childhood and adulthood cancers but there is paucity of literature on cancers among AYA.^{2,3} In our study, a total of 108 cases of proven cancers were diagnosed in patients aged 30 years or below accounting for 14.1% of all malignancies diagnosed which is less than 85.7% obtained in patients aged over 30 years. Majority of these cancer patients were in the 21-30 years age group (72.2%) which concurs relatively with mean and modal ages of 23.1 years and 30.0 years respectively. In USA, the annual incidence rate of cancer in children and adolescents was reported to be 186.6 per 1 million children aged 0 to 19 years.³ On the other, another study in North America recorded an increased incidence of cancer in AYA with a rise from 346 per million per year for those aged 20 to 24 years to 604 per million per year for those aged 25 to 29 years.⁴ These findings are further supported by a study conducted in Queensland, Australia which recorded varying incidences of cancers in relation to age group ranging from 0.6% in childhood (0-14 years) to 2.0% in adolescents and young adults (aged 15-29 years).⁵ This also compares relatively with findings from a study conducted in England and Wales where annual incidences of cancers ranged from 122 per million children aged less than 15 years to 150-200 per million adolescents aged 15-19 years.⁶ Findings from another study in UK indicated that the incidence of cancer in adolescents aged 15-19 years old is 50% higher than that in younger persons while rates in both males and females were significantly higher in persons

aged 20-24 years old than those aged 15-19 years old.⁷

From the foregoing, it is obvious that patients aged 30 years or younger are not spared by cancers. It has been proposed that this younger population exhibit features unique to their age group (15 to 29 years), including a distinct cancer epidemiology, evolving hormonal milieu, maturing development, transitions in autonomy, increasing demands in education, entry into the workplace and family responsibilities.^{4,5} In addition, lack of a well structured health insurance for this younger population is associated with delay in diagnosis which is worsened by the fact that most insurance companies in developing countries like ours are not interested in providing insurance coverage for patients with cancers owing to worse outcome and reduced survival rate. A study has also proposed that AYA have an exponential risk of developing cancer as they advance in age, thus suggesting a basic carcinogenic exposure that is age-dependent including telomerase shortening or a mutation-to-malignancy rate that increases constantly with age.⁸

Female preponderance with a male to female ratio of 1: 3.2 was recorded in our study which compares relatively with findings from a study in USA (F:M=1.6:1).² This however contrasts the finding of a slight male preponderance in studies conducted in USA and England and Wales (M:F=1.1:1 to 1.2:1).^{3,6,9} This gender disparity reported in most studies may be coincidental. However, certain cancers are sex-specific. In boys, the risk of testicular germ cell tumors is significantly higher in early childhood, and AYA aged above 15 years while ovarian germ cell tumors occur commonly in the post-pubertal girls.⁶ Furthermore, germ cell tumors are markedly more common in males than females in the older age groups while malignant melanoma is more common in females in those aged over 15 years, as are carcinomas of the thyroid, breast and genitourinary tract.⁶ For most sex-specific cancers, there is usual underlying dependence on pro-oncogenic hormones which bind to numerous specific receptors that abound the primary tissues, thus amplifying the process of oncogenesis. The most common cancers among children, adolescents and young adults (AYA) vary by age. In our study, embryonal cancer (50.0%) and Non-Hodgkin's lymphoma (18.8%) were the two leading cancers in children (0-14 years) while carcinomas of the breast (40.7%) and soft tissue sarcoma (13.0%) ranked first and second most common cancers among AYA; both of which were significantly higher in females within the 21-30 years age group. In contrast to our study, studies from Queensland, Australia, USA, England and Wales reported haematological and central nervous system cancers as the two leading

cancers in children.^{3,5,6} On the hand, most studies reported Hodgkin disease as the most common cancer in adolescents.^{3,5,7,8} In contrast to distribution of cancer in children and adolescents, malignant epithelial tumors (carcinomas) predominated in young adults.^{5,6} This however differ from findings from a study conducted in Queensland, Australia where melanoma was the most frequently diagnosed cancer (34%), followed by haematological cancers (19%) and urological cancers (10%) among adolescents and young adults (15-29 years).⁵ In variance to most studies, a study from Greece recorded Hodgkin's disease as the commonest cancer in young adults; this is followed by germ cell tumors, melanomas, CNS cancers, bone and soft tissue sarcomas.⁷ From the foregoing, it is obvious that distribution of cancer is age-specific and it is characterized by occurrence of genetically associated leukemia, central nervous system cancers and embryonal cancers in children, Hodgkin' lymphoma and germ cell cancers in adolescents; and epithelial cancers, Hodgkin's lymphoma and sarcomas in young adults. Besides genetic factors including chromosomal and gene disorders, environmental factors including ionizing radiation and aromatic hydrocarbon exposure, and cigarette smoking have also been implicated in the aetiopathogenicity of most cancers in childhood and AYA patients; these include cancers of the skin, gastrointestinal, lungs, breast, malignant lymphoma and leukemias.^{4,19} Unlike in most studies, cancers of the central nervous system were not reported in our study owing to non-availability of neurosurgical services. Thus, availability and affordability of highly specialized surgical services in different health care institutions also determine the type of cancers commonly diagnosed in different countries.

High grade cancers of breast and uterine cervix predominated among patients aged 0-30 years old in 61.4% and 50.0% of cases respectively. The majority (45.9%) of the breast cancer patients presented in advanced stages of the disease with regional lymphadenopathy (9.1%), ascites (6.8%) and distant metastasis (4.5 %). Available data from many studies have shown that the AYA patients with cancer tend to have worse prognosis when compared to childhood and pure adult cancers.^{18,19} This relatively poor prognosis in AYA patients have been proposed to be due to many factors including racial and ethnic disparities, lower socioeconomic status, poor parental education, poor health insurance status, untimely diagnosis, non-enrollment in cooperative group clinical trials, inadequate knowledge about the cancer diagnosis, poor quality of treatment and supportive care, differences in disease biology, genetic polymorphisms in the metabolism of chemotherapeutic drugs, and variations in adherence to therapy.^{3,18,19}

Rising incidence of malignant epithelial cancers including cancers of breast and uterine cervix among AYA patients is worrisome, thus, a well structured and expanded cancer screening protocols are suggested, commencing from age of menarche.

Conclusions

This study showed that embryonal cancer was the most common cancer in patients aged 0 to 14 years while carcinoma of the breast and soft tissue sarcoma were the two most common cancers in patients aged 5 to 30 years.

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