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Wilms' tumour in African children: Can an institutional approach improve outcome?

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ABSTRACT

Background: The poor outcome for patients with Wilms' tumour (WT) in developing countries has been predicated on late presentation, poverty and low rate of chemotherapeutic access. This study aims to evaluate the effects of an institutionalised approach to improving outcome for patients managed in a tertiary hospital in Nigeria. **Materials and Methods:** Oncology records of children diagnosed with WT between 2009 and 2013 were analysed for therapy completion and other prognostic parameters. Ensuing data were then compared with those from other centres in Africa. **Results:** Compared with results from some local and African studies, the therapy completion rate was higher (60%) with a survival rate among this group being between 1 and 4 years. No patient was lost to follow-up because of unavailability or unaffordability of cytotoxic agents. **Conclusion:** This study shows that an institutionalised approach can help to improve access to anti-cancer drugs, reduce the rate of loss to follow-up and thus improve outcome. There is however need to improve on patient-doctor communication, form support groups and establish a WT registry.

Key words: Chemotherapy, follow-up, outcome, survival, Wilms

INTRODUCTION

Wilms' tumour (WT), named after the surgeon Wilms[1] perhaps best epitomises challenges faced by paediatric oncologists and surgeons in developing countries. In developed countries survival rates of 70% to 90% have been achieved,[2,3] compared with African rates between 0% and 52.7%.[4-6] This poorer outcome has been attributed to late presentation,[5,7,8] inability to afford therapy,[4,8,9] and nonavailability of drugs.[4,7-9] Finding solutions to these impediments is thus vital.

This study, therefore, aims to evaluate the outcome of WT patients against a background of institutionalised measures put in place in a tertiary hospital to ensure survival.

MATERIALS AND METHODS

Oncology notes and histological slides of cases of nephroblastoma that were diagnosed and managed in a Teaching Hospital over a 5-year period between 2009 and 2013 were reviewed. Data retrieved included age, duration of symptoms before presentation to the clinic, stage at presentation, completion or otherwise of chemotherapy, duration of follow-up and outcome of the patient. Histologically grade, where available, were, also documented.

RESULTS

In the 5-year study period, 30 cases of biopsy proven nephroblastoma were diagnosed in our centre and centres from neighbouring states, but records of only 25 managed in our centre are discussed. These comprised 15 males and 10 females (ratio 1.5:1) with mean ages of 5.4 ± 1.0 year and 4.4 ± 2.2 years respectively. Only the case of bilateral tumour was seen, and even though 15 (60%) of the cases were left sided, with a $P = 0.767$, there was no statistically significant laterality.

Table 1 shows that 2 (8%) of the children presented in stage I; 1 (4%) in stage II; 16 (64%) in stage III; and 5 (20%) of the remaining children presenting in stage IV as well as a bilateral stage V case accounting for the remaining 4% of cases. There was no statistically significant relationship between age and stage or gender and stage ($P = 0.376$). Duration of preclinical presentation was 9 ± 5.0 months. 4 cases (16%) were

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ruptured at surgery and at histology classification according to the International Society of Paediatric Oncologists (SIOP) 2001[10] schema stratified 21 (84%) of the cases as intermediate risk.

Chemotherapy regimen is based on the SIOP-9 protocols. Vincristine and actinomycin D are given for 4 weeks prenephrectomy. Nephrectomy is then done within 1 week. For those that have immediate nephrectomy and pretreated cases, vincristine and actinomycin D are given for 18 weeks for stage I, while doxorubicin is added and given for 27 weeks for other stages, including radiotherapy, where finance is not a constraint, for stage III and above.

Table 1 also shows that five of the children were given pre- and post-operative chemotherapy while the remaining 20 were given chemotherapy only postoperatively in addition to nephrectomy. 15 (60%) of the children completed therapy while for various reasons the remaining 40% did not. 12 (86.7%) of the 15 are alive from periods ranging from 1 to 4 years. There were two relapses and these were referred for radiotherapy and continuation of therapy to another tertiary centre. The three who died out of the 15 include 1 who died of metastatic disease to the lung; and two who died from drug toxicity. Of the 10 who did not complete therapy, 2 were referred to other centres for continuation of therapy and follow-up because of distance to our centre; two were self-discharged by care giver against medical advice. Three of the remaining (6 of 10), died of metastatic disease (2 cases) and complications of chemotherapy (a case). With the exception of the two referred to another centre, and the assumption that those who did not complete treatment are dead, the survival rate in our centre would be 52% (12 of 23) cases.

Comparison of pertinent findings from other studies in the country is presented [Table 2]. The studies show that rate of completing therapy ranged from 3.7% to 42.9% compared to 60% in our centre.

Table 1: Characteristics of patients based on therapy

Outcome	Completed chemotherapy		Incomplete chemotherapy	Total (100%)
	Alive (52%)	Dead (12%)	Others* (36%)	
Pre- and post-operative chemotherapy	1	1	3	5 (20)
Post-operative chemotherapy only	12	2	6	20 (80)
Stage at diagnosis				
I-II	3	—	—	3 (12)
III	9	2	5	16 (64)
IV-V	3	1	2	6 (24)
Grade				
Low risk	2	—	—	2 (8)
Intermediate risk	10	2	9	21 (84)
High risk	—	—	2	2 (8)
Tumour rupture	1	2	1	4 (16)
Death from complications of therapy	—	2	4	6 (24)
Metastatic disease	—	1	3	4 (16)
p53 mutation	1	2	—	3 (25)

*Lost to follow-up, referred or discharged against medical advice

DISCUSSION

This study shows that as much as 60% of the children treated with chemotherapy in our study completed treatment with 81% being alive from 2009 till date; thus the likelihood of surviving is higher with completed therapy ($P = 0.001$). As concluded by Axt *et al.*[6] in Kenya ($P = 0.001$), Wilde *et al.*[9] in Malawi, as well as others in Nigeria,[4,5,7,8] the key to improving outcome among WT patients in resource-constrained countries of Africa is to ensure completion of therapy. These include efforts to ensure availability and affordability.

Even though the measures to be discussed hereon were not specifically put in place for only nephroblastoma patients, we believe these might have contributed to the survival among our patients.

Several factors contribute to decimating our patients' care-givers' resources before they present to the

Table 2: Comparison of features and outcome of WT patients from different local studies

Characteristics	Our study	Osuoji *et al.*[7]	Uba and Chirdan[4]	Ekenze *et al.*[5]	Abubakar *et al.*[8]
N	25	35	32	42	44
Age (mean) years	4.8	3.4	4.0	4.1	3.0
Male:female ratio	1.5:1	1.5:1	1.9:1	1.1:1	1:1.4
Duration of symptoms (mean) months	9.0	3.5	Late	4.7	Late
Predominant stage	III	III	IV	III	IV
Completed chemotherapy (%)	60.0	14.3	37.5	42.9	3.7
Outcome (alive >1-year)	52.0	14.3	18.8	23.5	Nil

WT: Wilms' tumour

hospital. Topmost among these is the healthcare-seeking behaviour of patients in our setting whereby nonorthodox practitioners, religious centres and patent medicine stores are primarily consulted before presenting to the hospital.[11,12] By the time, they present the disease would have progressed, and most of their resources would have been depleted. Fear of the high cost of treatment, possible hospitalization and consequent potential loss of wages appear to underlie this behaviour.[13]

The solution in our centre is to provide services, including sale of drugs, to all paediatric age groups at half of adult prices. Secondly, the drugs are purchased directly from representatives of companies that produce these drugs or import them, thereby eliminating the middleman and his added marginal cost. Thirdly the Drug Manufacturing Unit of the Pharmacy Department produces some paediatric medications which are then sold to patients at minimal marginal profit.

However, other far reaching measures need to be adopted. These include institutional evaluation of generics of branded anticancer drugs and if found efficacious to switch to these generics. This solution was adopted in a study in US resulting within a week in the reduction in the price of a branded anticancer drug by 50%.[14]

Apart from the high out-of-pocket expenditure that is associated with drug purchase, its availability, even when funds are available, is another factor that may militate against optimization of therapy. Osuoji *et al*.[7] and Uba *et al*.[4] in Nigeria and Wilde *et al*.[9] in Malawi also highlighted this factor as a contributor to poor outcome among their nephroblastoma patients.

Availability is enhanced in our institution by collaborations formed between our paediatric surgeons, clinical haematologist and representatives of drug companies that supply the anticancer drugs. This direct contact ensures the drugs are available as at when due. Response time is also shorter when there is a temporary shortage. Such collaborations between clinicians and oncology pharmacy specialists (where such are available) will go a long way in ensuring optimum cytotoxic drug procurement, administration, evaluation and monitoring.[15]

In our centre, the establishment of a drug revolving fund in the pharmacy department helps to ensure necessary drugs are available in the hospital including anti-cancer drugs. The effectiveness of this scheme in ensuring the availability of drugs has been demonstrated in parts of Nigeria and other parts of Africa.[16,17] The study by Ali[17] in the Sudan discusses how to establish and maintain such a scheme. In the same vein, the Partnership for Transforming Health Systems 2 scheme was established by the UK aid in the year 2008 with the objective of strengthening Nigeria's health system. It provides investments for initiating drug revolving funds across the country as well as technical support for intending centres.

Iravani[18] in a review of functions of social workers working with cancer patients succinctly captured their role as that of communication, support, assistance with funding and follow-up care. Unfortunately, as a reflection of the high poverty rate in most African countries, the role of social workers as fund-raiser has overshadowed their other equally indispensable roles. In our institution, after thorough scrutiny, they assist indigent patients by underwriting hospital bills. It sources its funds from philanthropic nongovernmental organisations, individuals and corporate bodies. It is also involved with acting as an intermediary between aid-seeking patients and local and state governments. The social welfare fund is also boosted by monthly deductions from profits made by revolving funds of other departments. This ensures that when there is donor fatigue the fund is always afloat. However, it takes a lot of hard work by members of the department, and dedication has been a major factor that has sustained the social work.

The other role of the social worker as an organiser of support groups for cancer patients is underplayed in our setting because of inadequate staff strength and overwork. The decision to discontinue therapy by the parents of two of our patients out of despair and hopelessness may also be a reflection of this lack of support groups and adequate counselling. One mother was divorced by her husband because of accrued cost of treatment for her child. Cancer-specific support groups are unexplored treasure troves that need to be incorporated into the care of patients in oncology centres in Africa. These will help to meet patients' emotional needs, share experiences with survivors and improve outcome for our patients, especially when overseen by experienced social workers.

In our centre, the paediatric surgical unit also supports cancer patients by an intraunit fund sustained by philanthropic donations chaperoned by the members of the unit. This greatly aided many of the indigent patients to complete their treatment.

In developing countries, especially in Africa, anxiety has been identified as one of the factors that underlie failure to show up for follow-up.[13] Long waiting times, anxiety about what to expect and long distances from the facility are some of the reasons for this.[19,20] Surveys of patients' satisfaction with ease of accessing services in tertiary hospitals in Nigeria showed a range between 41.2% and 84%.[21-23] These negative perceptions, coupled with other earlier mentioned factors, may underlie patients' resultant loss to follow-up.

This scenario can be mitigated by ensuring phone numbers of patients or their nexts of kin are documented by medical records department at the point of accessing services in the hospital. This is being practiced in our centre. Using this method dedicated oncology nurses and staff can directly contact patients or their care-givers to ensure compliance with medications, remind them of their appointments, guide them through their appointments and solve other sundry problems. Such a system's effectiveness has been shown by Dudas *et al.*[24] in their follow-up of patients after hospitalisation. Such telephone calls may help to obviate the need for physical follow-up and its attendant cost of transportation as well as help reduce lost man-hours at work of accompanying caregiver.

The caveat we have observed in our setting with phone calls is the cost and the observation that a number of caregivers and patients are not consistent with their phone lines.

Even though a survey of services in our centre showed that 88% of our patients were satisfied with the level of patient — provider interaction, only 46.2% felt interaction with our doctors was excellent.[23] One of the indicators of the robustness of doctor-patient interaction is the doctor's ability to communicate well with the patient and/or caregivers. Tongue *et al.*[25] showed that while 75% of a group of surveyed doctors felt they had satisfactorily communicated with their patients only 21% of the same patients reported satisfactory communication with the doctors. Okokon and Ogbonna[26] in a study in Calabar, Niger-Delta region of Nigeria, showed that the physician's attitude which most favourably influenced patients' perception of quality of treatment given were inclusion of patients in decisions about their care and showing care and concern about their condition. Thus, the outcome in cancer patients, perhaps more than in any others, will certainly be improved when oncology practitioners improve on their communication skills.

Ong *et al.*[27] summarised the priorities for cancer communication into three components:

1. Creating effective interpersonal processes,
2. Exchanging information and,
3. Facilitating appropriate treatment-related decisions.

Therefore, the clinician must be felt to be caring; pass information and listen to feedback from the patient and then involve the patient in decisions about their care. Failure to properly manage these components have been shown to culminate in unmet emotional needs,[28] hopelessness,[29] and poor adherence to follow-up.[30]

Another crucial strategy is to get treatment of cancers in general and paediatric cancers in particular on the list covered by health insurance providers. Neither our patients nor their care-givers were covered by the National Health Insurance Scheme. The positive effect of getting health insurance coverage for paediatric cancers is clearly demonstrated by an increase in 2-year event-free survival of WT patients in Kenya from 34.7% to 52.7%.[6,31] This improvement in outcome resulted from increased access to anti-cancer drugs because of improved coverage of paediatric diseases by the National Hospital Insurance Fund scheme in Kenya.[6,31] In some states in Nigeria free healthcare for paediatric age groups is provided, but, as noted by Ekenze *et al.*,[5] parents of the children still have to bear the cost of treatment for neoplastic diseases.

The Kenyan experience where collaboration was formed between Kenyan high-volume hospitals and the Vanderbilt University Medical Centre, Nashville Tennesse, has resulted in not only improvement in patient outcome, but also in molecular characterisation of their tumours as well as establishment of a WT Registry.[6] Such collaborative efforts are worthy of emulation for other centres in Africa where such is non-existent.

In summary, this study has shown that even though institutionalised measures aimed at improving outcome of patients in our centre has contributed to better outcome for our nephroblastoma patients, a lot more needs to be done individually, nationally and continentally to come up with innovative ideas, not limited to those discussed above, to improve prognosis in our cancer patients.

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