Outcomes Of Wilms' Tumour Management At The Paediatric Oncology Unit Of The Korle Bu Teaching Hospital

Turay I[1*], Oduro-Boatey C[1] , Ozoya O[2]

[1] Department of Paediatrics, Korle Bu Teaching Hospital, Accra, Ghana

[2] Department of Paediatrics, Family Health University College, Teshie, Ghana

***Corresponding Author: Ishmael Turay**
Address: Department of Paediatrics, Korle Bu Teaching Hospital, Accra, Ghana Phone: +233 20 1399308 Email: turayishmael@gmail.com

Abstract

Introduction: Wilms' tumour is a relatively common paediatric malignancy affecting children between 2 to 5 years of age. The survival rates for Wilms' tumour in the developed world is about 90-95% whereas the average in Sub-Saharan Africa is below 50%. The aim of the study was to determine the current outcomes of children managed for Wilms' tumour at the Korle Bu Teaching Hospital, Accra.

Methods: The folders of 57 children managed for Wilms' tumour at the Paediatric Oncology Unit between 1st January 2017 and 31st December 2019 were studied. Data extracted was analyzed with SPSS version 26 and statistical significance was set at 0.05.

Results: Of the 57 folders analyzed, there were 40 (70.1%) survivors and 17 (29.9%) deaths. Five (8.7%) patients relapsed following initial treatment for Wilms' tumour. The mean end of treatment survival was 67% and the average survival time was 294.6 (243.05-346.36) days. The log rank test did not show any significant difference in survival rates between male and female survivors. The average age of children with Wilms' tumour was 4.2 years (SD 2.6 years). The Cox regression model shows a 73% increase in the expected hazard for every year increase in age.

Conclusion: The average end of treatment survival for children treated for Wilms' tumour at the Korle Bu Teaching Hospital has increased over a 5-year period. A team of dedicated staff as well as financial commitment from partner organizations has made all the difference.

Keywords: Wilms tumour, outcomes, survival, childhood cancer

Introduction

Wilms' tumour also known as Nephroblastoma is the most common genito-urinary malignancy of childhood. It is responsible for about 8% of all childhood cancers in high income countries.[1] The frequency of occurrence in both males and females is 1:1. More than 70% of affected children are between the ages of 2 and 4 years. About 90% of affected children are under the age of 7 years.[1] Most children with Wilms' tumour present with asymptomatic abdominal distension. However, about a third of them present with abdominal pain, loss of appetite, vomiting, malaise or combination of all.[2] About 25% of patients present with hypertension and other congenial syndromes: The most recognized non- overgrowth syndrome is the WAGR - Wilms tumour, aniridia, genitourinary

malformations and mental retardation followed by Denys-Drash syndrome. 15-30% present with overgrowth syndromes such as Beckwith-Wiedemann depending on whether they have unilateral or bilateral disease.[2] Haematuria is present in about 30% of children diagnosed with Wilms' tumour and close to 10% are complicated by coagulopathy.[3] A retrospective chart review of patients treated for Wilms' tumour over a 3-year period spanning 2011 to 2013 in seven International Society of Paediatric Oncology (SIOP) supported treatment centres in Africa including Korle Bu Teaching Hospital [KBTH] reported average end of treatment survival to be 39%, with a range of 11% in Uganda and 61% in Malawi. The survival rates for Komfo Anokye Teaching Hospital and KBTH was 32% and 46% respectively.[4] This study sought to determine the current trend of presentation and outcomes of children managed for Wilms' tumour at the Paediatric Oncology unit of the KBTH. It is important to determine the stage at presentation and the prognosis of this condition as children who present late usually end up with a bad prognosis as a result of metastasis to vital organs like the lungs, liver, brain or bone marrow.

Methods

This was a retrospective chart review of cases managed between 1st January, 2017 and 31st December 2019 at the Paediatric Oncology unit, Department of Child Health, KBTH, which is the largest tertiary hospital in Ghana. Data extraction forms were used to collect the following information: sociodemographic characteristics, clinical presentation, risk factors, management, complications, relapse, treatment of relapse, follow up and outcome. All data collected was entered into Excel 2013 spread sheet and further exported to SPSS version 26 for analysis. Descriptive statistics was used to analyze demographics.

Overall survival for Wilms' tumour was determined using Kaplan Meier method with 95% Confidence interval. Log rank test was used to compare the equality of survival groups. Multivariate survival analysis using potential prognostic factors such as sex, age, and status of completing therapy was done using the logistic regression and Cox proportional hazard model on the survival data. Approval for the study was obtained from the Ghana College of Physicians and Surgeons and the Institutional Review Board of the Korle Bu Teaching Hospital Protocol number KBTH- IRB-000119/2020.

Results

Sixty-four patients were treated for Wilms' tumour between 1st January 2017 and 31st December 2019 at the Paediatric Oncology Unit, Department of Child health, KBTH. At the time of data collection, only 57 folders could be located (Table 1).

Table 1 Socio-demographic variables of participants

Variable	Frequency	Percentage
Age	Mean = 4.2	SD = 2.6
Sex		
Male	25	43.9
Female	32	56.1
Address		
Accra	29	50.9
Outside Accra	28	49.1
Region		
Accra	30	52.8
Volta	9	15.8
Central	6	10.5
Eastern	6	10.5
Northern	1	1.8
Brong Ahafo	1	1.8
Outside Ghana	4	7.0
School		
Nursery	11	19.3
Kindergarten	18	31.5
Primary	13	22.8
None	15	26.3
NHIS		
Yes	37	64.9
No	20	35.1

SD: standard deviation,
NHIS: National health insurance scheme

Clinical presentation

Most of the children 52 (91.2%) presented with abdominal distension. Twenty-one (36.8%) presented with abdominal pain, 18 (31.6%) had hypertension and 13 (36.8%) presented with haematuria. The average length of time before presentation to the Paediatric Oncology Department was 12.3 weeks, with a standard deviation of 9.7 weeks (Table 2).

Table 2 Descriptive statistics of clinical presentation

Presentation	Length of presentation	Frequency	Percentage
Abdominal distention	Mean = 12.29	SD=9.7	
Yes		52	91.2
No		5	8.8
Abdominal pain	Mean = 13.38	SD=5.6	
Yes		21	36.8
No		36	63.8
Hypertension	Mean = 8.00	SD=0.0	
Yes		18	31.6
No		39	68.4
Haematuria	Mean = 4.60	SD=4.34	
Yes		13	22.8
No		44	77.2
Weight loss			
Yes		21	36.8
No		36	63.2
Others			
Yes		24	42.1
No		33	57.9

SD: Standard deviation; Length of presentation in weeks

Presentation and Duration of Treatment

The average time taken from presentation to commencement of treatment was 16.75±4.58 days while the average time from commencement of treatment to the end of treatment was: 202.39 (SD=22.54) days. The average time taken from commencement of treatment to the demise of a child was 268.23 days (SD= 20.16) days.

Presentation and treatment outcomes

Out of the 57 children who presented with Wilms' tumour for the period under review, there were 17 deaths (29.8%, 9 females and 8 males) and 40 survivors (70.2%, 23 females and 16 males). The average survival time for patients treated for Wilms' tumour was 294.6 (243.05-346.36) days, with the median time being 380 (277.64-48235) days. Females seemed to have had higher survival than male children: 268 (146.79-389.20) and 380 (41.07-718.92) days for median survival time between males and females respectively whilst mean survival time was 249.45 (187.04-311.87) and 328.20 (270.69-385.71) days for males and females respectively. There was however, no statistical significance by the log rank test performed to compare gender and survival outcomes. Within the first 100 days, 84% of the patients survived and the proportion of patients who survived within this time interval was approximately 67 %. This is also illustrated by the Kaplan Meier curves in figure 1.

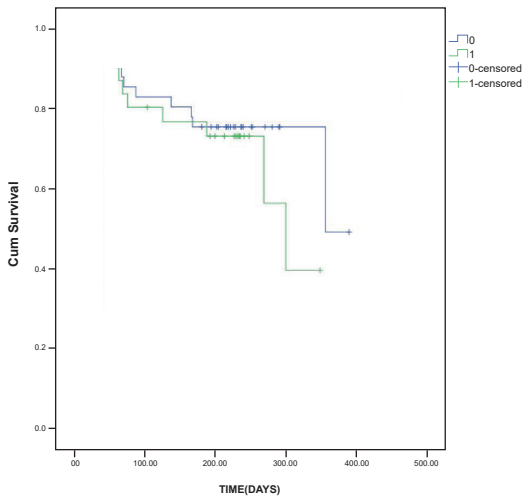

Figure 1 Kaplan-Meier survival distribution

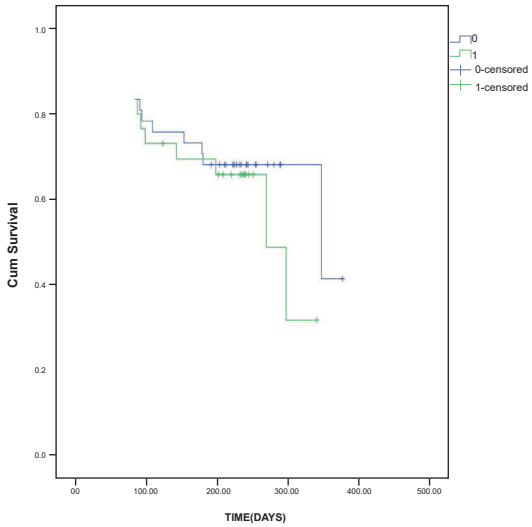

Figure 2 Kaplan-Meier gender survival distribution

Note: Kaplan-Meier survival curves for patients treated for Wilms' tumour (1= male, 0 = female)

Risk of Mortality

The Cox regression model illustrates a 73% increase in the expected hazard for every yearly increase in age. The risk of dying of Wilms' tumour was 3.36 times higher in patients who presented with haematuria. Also, for every unit increase in the WBC, the risk of dying increased by 1.12. There was a significant association between the death of a patient as a result of Wilms' tumour and their age, WBC, platelets and the presence of hematuria.

Table 3 Cox regression of independent variables and outcome

Variable	Hazard	Confidence interval	P value
Age	0.73	0.53-10.1	0.05
Female	2.16	0.67-7.02	0.19
NHIS	2.78	0.67-11.4	0.15
Haematuria	3.36	0.99-11.31	0.05
Platelet count	0.99	0.98-0.99	0.00*
WBC	1.12	1.03-1.23	0.01*

Distribution of treatment, complications and outcome

In terms of risk assessment, 25 (43.9%) of the respondents had low risk disease, 16 (28.1%) had intermediate and 15 (26.3%) had high risk disease. None of the patients refused or abandoned treatment. Treatment was classified as palliative or curative. All patients had chemotherapy and some had additional treatment such as radiotherapy and or surgery (Table 4). Twenty patients, presented with various forms of complications, commonest was febrile neutropenia followed by severe anaemia (Table 4). There were 5 (8.7%) patients who relapsed following initial treatment for Wilms' tumour.

Table 4 Distribution of treatment complications and outcome

Variables	Frequency	Percentage
Treatment		
Curative	48	84.2
Palliative	9	15.8
Refuse treatment	0	0
Management		
Chemotherapy	15	26.3
Chemotherapy+ surgery	34	59.6
Chemotherapy+ surgery+ radiotherapy	8	14
Complication		
Febrile neutropenia	9	45
Severe anaemia	5	25
Electrolyte imbalance	3	15
Sepsis	2	10
Respiratory distress	1	5
Relapse	5	8.7
Outcome		
Alive	40	70.2
Death	17	29.9

Discussion

Findings of this study indicate that among fifty-seven children treated for Wilms tumour the mean age was nearly four years. These figures compare to a similar study by Ko and Ritchey who reported that more than 80% of cases of Wilms' tumour were diagnosed before the age of 5 years and that the median age of presentation was 3.5 years.[5] Majority of our patients (56.1%) were females, unlike a study by Israels et al in Malawi who found 53.4% of their patients to be males[6].

About 9% percent of the patients relapsed following initial treatment for Wilms' tumour which was lower than the 15% reported by Malogolowkin, et al. Most of these relapses occurred in the first 2 years of diagnosis.[7] Twenty-nine (50.9%) out of the 57 patients resided within Greater Accra metropolis and 64.9% of respondents had National health insurance (NHIS). Empirical evidence shows that financial capability plays a significant role in completion of cancer treatment and thus, funds made available by the Wilms' tumour project funded by the World Child Cancer enabled most of the patients to complete their treatment. Many patients do not complete treatment for cancer as a result of poverty.[2]

The rate of 'abandonment' of treatment ranges from 14-48%and it is the most common cause of treatment failure or death in low-income countries.[2,6,8] From the study, the most common presentations among the children were abdominal distension, abdominal pain, hypertension, and haematuria. A study conducted by Abu-Idris et al opined that there were no specific clinical features attributable to Wilms' tumour. In their study painless abdominal distension was the commonest clinical presentation in about two-thirds of participants. In the same study, about 30% of patients presented with abdominal pain, anorexia, vomiting, malaise or a combination of all and 25% present with hypertension. The risk of dying of Wilms' tumour is three times higher in patients who present with haematuria.[2]

Increase in age and white blood cell (WBC) count also significantly increased the risk of mortality. In terms of risk assessment, half of the respondents had low risk disease, whiles the other half were at intermediate and high risk, unlike a study conducted by Borgstein et al which revealed that very few had a low-risk disease and majority i.e. nearly ninety-five percent experienced intermediate and high-risk of Wilm's tumour.[9] This is because in Ghana most Wilm's tumour cases are reported at early stages and most parents are educated thus they often seek for clinical attention when they see changes in their children. For the period under review, there were seventeen deaths and forty survivors, nearly one-third died (29%) compared with the reported death rates for Wilm's tumour; 13 to 37% percent depending on the treatment centers in Sub-Saharan Africa.[10] Late presentation to treatment centers, severe acute malnutrition and advanced disease are the major factors responsible for such untimely deaths. Low- intensity treatment protocols, optimal support staff and affordable intensive care units are all relevant in the prevention of treatment-related deaths.[10] From the study, the proportion of patients who survived within this time interval was approximately 67%. The average end of treatment survival in the collaborative Wilms' tumour African project was 39%, with a range of 11% in Uganda and 61% in Malawi.[4] The survival rates for both KATH and KBTH were 32% and 46% respectively[4].

These values are far lower than the results obtained from this current study.[11] This increase in survival outcomes can be largely attributed to the funds received by the cancer unit, education to the public and improved health service lately provided in the Oncology Department of the Korle Bu Teaching Hospital. From the study, survival of Wilms tumor has significantly increased over the years and further research is needed to identify steps that can be taken to further reduce the mortality rate of Wilms tumour. Collaborative activities like the collaborative Wilms tumour Africa project needs to be conducted in various SIOP-supported centres to raise funds to support families burdened with financial constraints. Sensitization on the common symptoms of childhood cancer should be intensified

so that patients can report to the hospital earlier to help with early diagnosis and treatment before tumour metastasis takes place.

Conflict of interest

The authors declare that they have no competing interests.

References

1. Hasanbegovic E, Sabanovic S. The results of wilms tumor treatment in children in the period 1998-2007. Folia medica facultatis medicinae universitatis saraeviensis. 2008 dec 1;43(2).
2. Abuidris DO, Elimam ME, Nugud FM, Elgaili EM, Ahmed ME, Arora RS. Wilms tumour in sudan. Pediatric blood & cancer. 2008 jun;50(6):1135-7.
3. Kalapurakal JA, Dome JS, Perlman EJ, Malogolowkin M, Haase GM, Grundy P, Coppes MJ. Management of wilms' tumour: current practice and future goals. The lancet oncology. 2004 jan 1;5(1):37-46.4.
4. Paintsil V, Renner L, Hesseling P, Burns L, Kambugu J, Amoah M, Kouya F, Haileyesus D, Molyneux E, Israels T. Abandonment of treatment at baseline in the collaborative wilms tumour africa project: pd-081. Pediatric blood & cancer. 2015 nov;62.
5. Ko EY, Ritchey ML. Current management of wilms' tumor in children. Journal of pediatric urology. 2009 feb 1;5(1):56-65
6. Israëls T, Chirambo C, Caron H, De Kraker J, Molyneux E, Reis R. The guardians' perspective on paediatric cancer treatment in malawi and factors affecting adherence. Pediatric blood & cancer. 2008 nov;51(5):639-42.
7. Malogolowkin M, Cotton CA, Green DM, et al.: treatment of wilms tumor relapsing after initial treatment with vincristine, actinomycin d, and doxorubicin. A report from the national wilms tumor study group. Pediatr blood cancer 2008, 50:236– 241.
8. Mostert S, Arora RS, Arreola M, Bagai P, Friedrich P, Gupta S, Kaur G, Koodiyedath B, Kulkarni K, Lam CG, Luna-Fineman S. Abandonment of treatment for childhood cancer: position statement of a siop podc working group. The lancet. Oncology. 2011 jun 28;12(8):719-20.
9. Israels T, Borgstein E, Pidini D, Chagaluka G, De Kraker J, Kamiza S, Molyneux EM. Management of children with a wilms tumor in malawi, sub-Saharan Africa. Journal of pediatric hematology/ oncology. 2012 nov 1;34(8):606-10.
10. Day S, Hollis R, Challinor J, Bevilacqua G, bosomprah e. Baseline standards for paediatric oncology nursing care in low to middle income countries: position statement of the siop podc