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Survival Outcome of Wilms Tumor with Multi-Modality Treatment at Jimma Hospital, Southwest Ethiopia

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Abstract

Background: Wilms' tumor (WT), the most common malignant neoplasm of the urinary tract of children [1], accounts for 5.9% of childhood cancers and affects one in every 10,000 children worldwide before the age of 15 years. The care of children with Wilm's tumor in sub-Saharan Africa is compromised due to resource deficiencies that range from inadequate healthcare budgets to paucity of appropriately trained personnel. Childhood Wilms tumor is surging as an important paediatric problem in developing and sub-Saharan Africa countries. The objective of the study is to establish an understanding on the treatment challenges and outcomes of Wilm's tumor in South West Ethiopia. **Results:** Forty-three Wilm's tumor patients who were admitted from January 2017 to December 2021 were included in the study. The most frequent presentation was painless abdominal swelling in 40 (93%) patients. Fourteen patients (32.6%) were hypertensive at the time of diagnosis and the other 13 (30.2%) were normal. In abdominal examination, 31 (72.1%) patients had abdominal mass not crossing the midline and 12 (27.9%) had mass crossing the midline. After multimodal treatment, 37.5% had improvement, 11.6% came back with relapse. Most patients (41.7%) abandoned treatment and 9.3% of the cohort died in the course of treatment. **Conclusion:** The outcomes in the treatment of Wilms Tumor have been found to be poor in this review. The main reason for poor outcome has been not receiving adequate chemotherapy after surgery. Doses of chemotherapy received after surgery significantly affected treatment outcomes ($p = 0.026$).

Keywords

Wilms, Survival, Treatment, Childhood Tumor

1. Background

Wilms' tumor (WT), the most common malignant neoplasm of the urinary tract of children [1], accounts for 5.9% of childhood cancers and affects one in every 10,000 children worldwide before the age of 15 years. [2] It is an embryonal neoplasm of the kidney in which blastemal, stromal and epithelial cell types are present in variable proportions [3].

In most pediatric malignancies, the survival rate of Nephroblastoma Wilms' tumor (WT) patient has noticeably improved with modern multidisciplinary cancer management [4]. The care of children with Wilm's tumor in sub-Saharan Africa is compromised due to resource deficiencies that range from inadequate healthcare budgets to paucity of appropriately trained personnel. It is also crippled by scarce laboratory facilities and inconsistent drug supplies making the outcome of this tumor in this setting still poor. All these factors contribute to less than 50% survival at 5 years as most studies report [5].

Patients face difficulties accessing healthcare, affording investigational and treatment protocols, and attending follow-ups. Children routinely present with advanced local and metastatic disease because of which many children cannot be offered any effective treatment. Multiple comorbidities, such as malaria, tuberculosis, and HIV in malnourished patients raise the chance of treatment-related toxicities. Survival rates are invariably poor [5] [6].

Pediatric surgical oncology is not yet regarded as a health care priority by many governments in the region and they are still struggling to achieve the millennium goals [6] Delayed diagnosis, poor compliance to treatment, and lack of multidisciplinary team for selection and stratification of patients prior to the commencement of management also contribute to the poor outcome [7].

Childhood Wilms tumor is surging as an important paediatric problem in developing and sub-Saharan Africa countries [8]. Besides these, there is a great burden of it with the disease being detected in its locally and distally advanced stages when appropriate chemotherapeutic drugs and surgical interventions will be neither available nor effective at all. Childhood solid tumors are becoming responsible for most deaths occurring in the first fifteen years of life [7]. Additionally, comorbidities that coexist along with the malignancy will compound treatment-related toxicities which directly impairs their adherence and effectiveness of the regimen provided with its attending risk of poor survival [5] [9].

The objective of the study is to establish an understanding on the treatment challenges and outcomes of Wilm's tumor in Southwest Ethiopia. It also lays the ground to possibly develop our own protocol or at least adopt protocols from developed countries for the proper and consistent management of Wilm's tumor.

2. Methods

The study was conducted at Jimma University Medical Centre (JUMC) South west Ethiopia, which is one of the oldest public hospitals in the country with a

bed capacity of 800. Geographically, it is located in the city of Jimma, 352 km southwest of Addis Ababa. It was facility based retrospective cross-sectional study; the study was conducted from January 2017

2.1. Study Design and Period

Facility based retrospective cross-sectional study; the study will be conducted from January 2017 through December 2021.

2.2. Source Population

All children admitted to JUMC, pediatric oncology unit, from January 2017 through December 2021 will be the source population

2.3. Study Population with Eligibility Criteria

All 43 patients with Wilm's tumour who were admitted to JUMC from January 2017 to December 2021 were included.

SPSS version 26 was used for data entry and analysis.

Permission and approval letter from the Ethical Review Committee of the College of Medicine and Health Science was obtained prior to the study.

3. Result

3.1. Clinical Characteristics of the Patients

A total of 46 patients were diagnosed with Wilms' tumor between January 2017 and December 2021. Three cases were excluded from the study because three of them didn't receive any form of therapy. The most frequent presentation was painless abdominal swelling in 40 (93%) patients. Painful abdominal swelling occurred in 3 (7%) patients. Gross hematuria, weight loss and cough were the other less frequent additional symptoms, constituting as chief complaint, in only 3 (6.9%). The median duration of presenting complaints was 1 month (range 0.06 - 30 months). Seventy-five percent of patients presented within 2 months of their symptoms and 8 (18%) patients presented after 3 months of their illness (Table 1).

The nutritional status was judged with anthropometry, 13 (30.2%) patients were malnourished and 30 (69.8%) were having normal anthropometry.

Fourteen patients (32.6%) were hypertensive at the time of diagnosis and the other 13 (30.2%) were normal. On abdominal examination 31 (72.1%) patients had abdominal mass not crossing the midline whereas 12 (27.9%) had mass crossing the midline.

3.2. Laboratory and Imaging Findings

Hemoglobin, platelet count and renal function were assessed at admission, 27 (62.8%) were anemic and 21 (48.8%) had thrombocytosis and all had normal renal function testing. All patients had undergone imaging with either US or CT scan of the abdomen. Among this ultrasound alone was done for 16 (37.2%)

Table 1. Clinical characteristics of patients with WT.

Variables	Frequency	Percentage
Presenting Symptoms		
Abdominal Swelling	40	93
Abdominal Pain	3	7
Additional Symptoms		
Haematuria	1	2.3
Weight Loss	1	2.3
Cough	1	2.3
Blood Pressure		
Normal	13	30.2
Hypertensive	14	32.6
Not Documented	16	37.2
Abdominal Findings		
Palpable Mass		
Not Crossing the Midline	31	72.1
Crossing the Midline	12	27.9
Anthropometry		
MAM	2	4.6
SAM	10	23.3
Normal	31	72.1

patients and CT alone for 4 (9.3%) patients and both US and CT scan for 23 (53.5%) patients. Sixteen (37.2%) patients had right sided tumor and 27 (62.8%) patients had left side tumor and no cases of bilateral disease or WT in a solitary kidney. The mean size was 13.8 cm (Range 7.4 - 21 cm) and two (4.3%) patients were diagnosed to have liver metastasis. Chest x-ray was performed for all patients before the commencement of the treatment and lung metastasis was diagnosed in one (2.3%) patient. Seventeen patients (39.5%) had localized disease (Stage I) and 23 (53.5%) had locally advanced tumor (Stage II & III) with the rest 3 (7%) having metastatic disease to liver and lungs (Stage IV) (Table 2).

3.3. Follow-Up and Outcomes

Length of follow-up varied from 0.5 to 40 months with a mean of 8.4 months. Totally, of 43 patients 16 (37.2%) patients had clinical improvement, 18 (41.8%) patients abandoned their treatment. Five (11.6%) tumor recurrences and 4 (9.3%) deaths occurred. One patient died while being operated due to cardiac arrest and the other 3 died due to the tumor itself (Table 3).

Table 2. Laboratory and radiologic characteristics of patients with WT.

Variables	Frequency	Percentage
CBC: Normal Haemoglobin	16	37.2
Anaemic	27	62.8
Normal Platelet Count	22	51.2
Thrombocytosis	21	48.8
U/A: Haematuria		
Positive	4	9.3
Negative	19	44.2
Not Documented	20	46.5
U/A: Proteinuria		
Positive	5	11.6
Negative	18	41.9
Not Documented	20	46.5
Creatinine: Normal	43	100
Abdominal US	16	37.2
Abdominal CECT	4	9.3
Abdominal US + CECT	23	53.5
CXR	43	100
Chest CT	0	0
Tumor Size		
5 - 10 cm	8	18.6
10 - 15 cm	20	46.5
15 - 20 cm	14	32.6
>20	1	2.3

Table 3. Outcomes of WT management at JUMC, Jimma (2017-2021).

Outcomes	Frequency	Percentage
Clinically Improved	16	37.2
Relapses	5	11.6
Treatment Abandonment	18	41.8
Death	4	9.3

From those who were clinically improved, 50% of them were on follow up for more than 6 months from diagnosis. All deaths occurred within 4 months of diagnosis. The treatment abandonment rate is 41.8% but no reason was found.

Events that were used to measure survival were death, recurrence and lost to follow-up. The 1-year event free and overall survival in those who took more than average cycles of chemotherapy were between 35% and 50% and between 20% and 40% respectively (Figure 1).

4. Discussion

There are no data on the incidence of WT and other solid tumors in Ethiopia. The frequency of childhood cancer is alarmingly increasing over years. It could be due to the increased public awareness and the health seeking behavior of the community. Wilms tumor is the second most common solid tumor of childhood [6]. The mean age at diagnosis was 45.2-months (median 36-month, range 5 to 156-months), 75% of the patients were younger than 60-months old, then after the incidence steadily decrease with age. These findings were close to the findings of a study in Nicaragua, where the median age at diagnosis was 36 months (range 9.6 - 96 months) and in Malawi, where the mean age at diagnosis was 50.4 months (range 10 - 158.4 months). [8] This was a tumor of younger age and other studies conducted in Taiwan had shown similar results. [9] Another study, conducted in Rwanda, where a different result was found, and the median age at diagnosis was 96 months (range 12 - 120 months) [10].

Histologic report after nephrectomy was documented for 17 patients. Most of the patients had favorable histology in 16 (94%) patients and unfavorable histology with diffuse anaplasia in 1 (6%) patient. This finding was comparable to the findings of a study conducted in Tanzania where 90% and 10% distribution of favorable and unfavorable histologies were reported respectively [11]. But in case of Egypt, the unfavorable histology was a bit higher (33%) as compared to our finding and that of Tanzania [11].

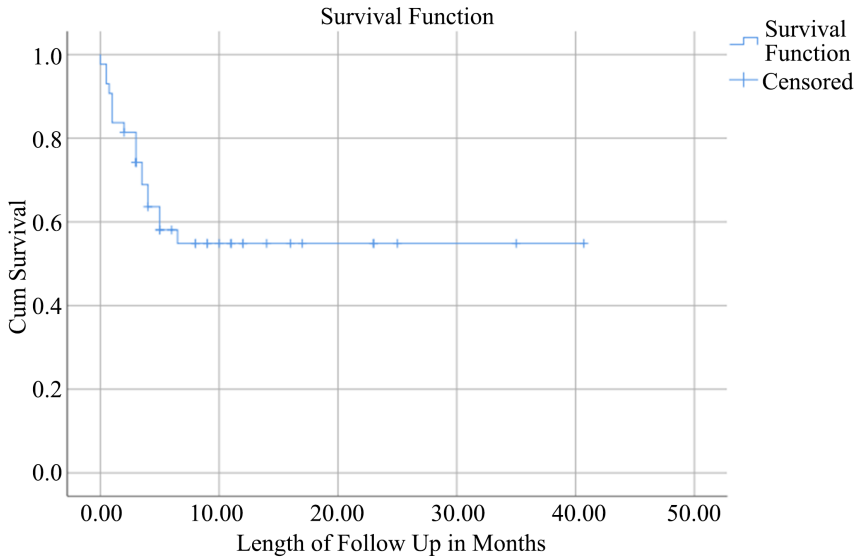

Figure 1. Kaplan Meier survival curve of patients with Wilms tumour after treatment in JUMC, Jimma Southwest Ethiopia (p = 0.026) NB. Crosses (+) indicate censored patients.

No statistically significant relationship with outcome was found for gender (p = 0.581), duration of illness (p = 0.208), tumor size (p = 0.49), nodal status (p = 0.521), stage at presentation (p = 0.764) and the protocol used (p = 0.476). The statistically significant variable which positively influenced the outcome was the number of post-operative chemotherapy doses received (p = 0.026). This finding was in contrary to the findings of other studies conducted in majority of African countries, in which disease stage at presentation and tumor volume were prognostically more important. The type of protocol used didn't affect the EFS or the OS of patients with Wilms' tumor but the postoperative dose of chemotherapy did (p = 0.026). Kaplan-Meier method was applied to estimate the probability of cumulative survival, EFS and OS. No patient had reached the median survival. EFS were measured from date of diagnosis of treatment failure or last follow-up and OS was measured from date of diagnosis to death and lost to follow-up. The 1-year event free and overall survival in those who took more than average cycles of chemotherapy were between and between 20% and 40% and 35% and 50% respectively. Findings were similar to other African studies where the 8-months overall survival was nearly 40%, [12] except in Sudan where their OS was 11% [13]. However, it has still been less than that of western countries where survival is greater than 90%. [8] [14] [15]. Survival in Europe during 1930s, when only nephrectomy was available as a treatment option for WT, was approximately 30% [13] [16].

5. Conclusion

The outcomes in the treatment of Wilms Tumor have been found to be poor in this review. The main reason for poor outcome has been not receiving adequate chemotherapy after surgery. Doses of chemotherapy received after surgery significantly affected treatment outcomes (p = 0.026). However, age at diagnosis, gender, and duration of symptoms, stage at diagnosis, and the protocol used did not predict survival. We therefore recommend that awareness creation on use of preoperative and postoperative chemotherapy could bring about better changes in mortality and morbidity of Wilms tumor patients. Other factors such as age, duration of symptoms and stage diagnosis were not related to better outcome significantly. Further large studies are needed to establish the factors affecting treatment outcome in developing center like ours, especially giving an emphasis to reduce treatment abandonment.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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