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Research Article

Outcome of Wilm's Tumor in Children – An Observational Study from Bangladesh

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Abstract: ***Introduction:*** Wilms' tumor or nephroblastoma is an embryonal tumor of childhood. Wilms tumor being the most common primary renal malignancy in children accounts for 5% of childhood malignancies. This study aimed to assess the outcome of Wilms tumor in children who underwent nephroureterectomy after neoadjuvant chemotherapy and evaluate the influence of the stage of disease on treatment outcomes. ***Methods:*** This was a retrospective observational study conducted in the Department of Paediatric Surgery, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh during the period from January 2012 to July 2015. In our study, we included 30 pediatric patients diagnosed with Wilms tumor who underwent nephroureterectomy at our institution. ***Result:*** We found the mean age was 39.5 ± 14.3 months. The majority (63%) of our study patients were male compared to female (37%). Of all 30 patients, 40% were diagnosed with low-stage (stage I to II) disease, and 60% were diagnosed with high-stage (stage III to stage V). The patients with low-stage (stage I to II) disease had a 100% survival rate, whereas the patients with high-stage (stage III to stage V) disease had a 44% survival rate. Among all patients, 22(73%) patients had favorable histology, while 8(27%) patients had unfavorable histology. ***Conclusion:*** In our study, the postoperative results were uneventful and the recurrence of symptoms or any other complaints was not observed in any case. The earlier stage of the disease and favorable histology had a higher chance of cure compared to the late stage of the disease or unfavorable histology.
Keywords: Children, Malignancy, Wilms' tumor, Chemotherapy, Outcome.

INTRODUCTION

Childhood illnesses are the most common cause for concern. While infectious diseases continue to be the primary focus, malignancy, which is historically viewed as a dreadful condition, is becoming a concern. [1] Despite numerous breakthroughs in disease diagnosis and treatment, pediatric malignancies continue to pose a substantial challenge to medical professionals, particularly in developing countries due to a lack of financing, the advanced stage of the disease, general ignorance, and poverty. [2] Childhood renal tumors account for approximately 6% of all pediatric malignancies. [3] Wilms tumor is the most common primary renal malignancy in children. It accounts for 5% of childhood malignancies.[4] Most of the patients are asymptomatic; they are usually diagnosed incidentally as a painless lump by parents or by physicians in routine checkups.

Wilms' tumor or nephroblastoma is an embryonal tumor of childhood. This constitutes the commonest intraabdominal solid tumor of childhood occurring at 1 in 100000 children younger than 15 years and the male-to-female ratio is almost equal. [1,5,6] The peak age of incidence is approximately 3-4 years. It presents usually in a healthy child as a painless abdominal mass. Other presentations like hematuria, anemia, or weight loss also may be the features. [2,7]

The management of Wilms tumor remains a matter of great challenge to pediatric surgeons and also to pediatric oncologists. The tumor continues to be the focus of rigorous investigations that, with the assistance of co-operative procedures by the National Wilms Tumor Study (NWTS), have resulted in considerable improvement in survival.[8] Survival rates have improved from 20% in the 1960s to approximately 90% currently in high-income countries; middle-income countries have survival rates of approximately 80%.[9] This has been achieved through cooperative study groups as well as the use of multimodal approaches to therapy. Low-income countries, however, have survival rates between 20% and 50%. [4,9,10]

Treatment for Wilms tumor includes surgery and chemotherapy, as well as radiotherapy for

metastatic disease. [9-11] Surgical excision remains the cornerstone of treatment of Wilms tumor; however, the dramatic improvement in overall survival is the result of coordinated use of surgery, chemotherapy, and radiation therapy. [7] The management of advanced cases of Wilms tumor is even more challenging. These include bilateral tumors, tumors with intracaval and atrial extension, advanced local tumors as inoperable and nonresectable ones, and distal metastatic tumors. The diagnosis as well as treatment of these cases remains a matter of great difficulty. Multimodal treatment especially preoperative chemotherapy may reduce the extent of the disease which ultimately may help in further surgical excision- total or partial, reducing the morbidity and mortality of the disease. [12] Preoperative chemotherapy may cause shrinkage of the tumor before resection. [8] In the event, that the tumor is too large or the child is too sick for surgery, a needle biopsy should be performed, and the tumor considered at least stage III for the treatment. [8]

In this study, we aimed to assess the outcome of Wilms tumor in children who underwent nephroureterectomy after neoadjuvant chemotherapy and evaluate the influence of the stage of disease on treatment outcomes.

METHODOLOGY AND MATERIALS

This was a retrospective observational study conducted in the Department of Paediatric Surgery, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh during the period from January 2012 to July 2015. In our study, we included 30 pediatric patients diagnosed with Wilms tumor who underwent nephroureterectomy at our institution.

These are the following criteria to be eligible for enrollment as our study participants: a) Patients aged up to 6 years old irrespective of sex; b) Patients having tumors with intracaval and atrial extension; c) Patients having non-resectable tumors (size more than 10cm X 9cm, with ultrasonographic evidence); d) Parents who were willing to participate were included in the study And a) Patients with a non-WT renal tumor; b) Patients with recurrent tumors; c) Patients not capable of withstanding chemotherapy; d) Patients with any history of acute illness (e.g., pancreatic diseases, ischemic heart disease, asthma, COPD, etc.) were excluded from our study.

Data Collection

After admission detailed history and physical examination were done and the results were recorded in the questionnaire. Investigations like routine blood and urine examination with renal function tests (RFT), liver function tests (LFT), ultrasonography (USG) of the whole abdomen with particular attention to the kidneys, liver and lymph nodes, plain X-ray abdomen, chest X-ray and CT scan of the abdomen in pre and post-chemotherapy state were done for all patients. Preoperative chemotherapy was given for four weeks with vincristine and actinomycin D according to SIOP protocol (Herdrich K, 1982).[2] The patients were followed up every 2 weeks by USG, LFT, Hb%, and chest X-ray for one month. The size of the tumor as well as the metastatic lesions in the prechemotherapeutic and post chemotherapeutic ultrasonographic findings was compared after one month. All the resected specimens were sent for histopathological studies.

Statistical Analysis

All data were recorded systematically in preformed data collection form. Quantitative data was expressed as mean and standard deviation and qualitative data was expressed as frequency distribution and percentage. The relationship between treatment outcomes and tumor stages was analyzed using the chi-square (X^2) test and Fisher's exact tests. A p-value <0.05 was considered as significant. Statistical analysis was performed by using SPSS 16 (Statistical Package for Social Sciences) for Windows version 10.

RESULTS

Table 1: Distribution of Our Study Subjects by Baseline Characteristics

Characteristics	N=30	P (%)
Age (years)		
0-2	4	13.33
>2-4	19	63.33
>4-6	7	23.33
Mean age (months)	39.5 ± 14.3	
Mean weight (kg)	16.65 ± 4.3	
Gender		
Male	19	63.33
Female	11	36.67
Type of Wilms' tumor		
Local tumors	22	73.33
Advanced tumors	8	26.67
Stage of Wilms' tumor		
Stage I	5	16.67

Stage II	7	23.33
Stage III	10	33.33
Stage IV	5	16.67
Stage V	3	10.00
Metastases		
Lung	22	73.33
Liver	4	13.33
Other sites	4	13.33
Laterality		
Right	11	36.67
Left	19	63.33
Clinical presentation		
Anorexia/weight loss	21	70.00
Hypertension	12	40.00
Hematuria	11	36.67
Abdominal pain	6	20.00
Mean Blood loss (ml/kg)	8.45 ± 4.75	
Mean Operating time (min)	125.83 ± 54.89	

Table 1 shows the baseline characteristics of our patients. We found the mean age was 39.5 ± 14.3 months. Most of our patients (63.33%) were aged >2 to 4 years old. The majority (63%) of our study patients were male compared to female (37%). Among our patients, most of the patients (73.33%) had local tumors and 26.67% had advanced tumors. Of all 30 patients, 40% were diagnosed with low-stage (stage I to II) disease, and 60% were diagnosed with high-stage (stage III to stage V). The mean operation time was 125.83 ± 54.89 minutes and the mean blood loss was 8.45 ± 4.75 ml/kg. Anorexia/weight loss was seen in the majority of patients.

Table 2: Tumor Parameters of Our Study Subjects Before and After Chemotherapy

Parameters	Before chemotherapy	After chemotherapy	P-value
Tumor depth (cm)	9.62 ± 1.41	7.59 ± 2.34	0.024
Tumor height (cm)	9.51 ± 2.50	7.32 ± 3.44	0.041
Tumor weight (gm)	834.33 ± 501.76	274.74 ± 129.17	0.014
Tumor volume (cm^2)	1064.28 ± 610.24	596.73 ± 637.48	0.023

Table 2 shows that tumor depth was 9.62 ± 1.41 cm before chemotherapy, and it decreased to 7.59 ± 2.34 cm after chemotherapy. Tumor height was 9.51 ± 2.50 and 7.32 ± 3.44 cm in before & after chemotherapy respectively. Tumor weight was 834.33 ± 501.76 gm before chemotherapy which reduced to 274.74 ± 129.17 cm after chemotherapy.

Table 3: Distribution of Our Study Subjects by Outcome

Stage of Wilms' tumor	Outcome, n (%)			Survival rate (%)
	Cure	Relapse	Death	
Stage I (n=5)	5	0	0	100%
Stage II (n=7)	7	0	0	100%
Stage III (n=10)	6	4 (40%)	0	60%
Stage IV (n=5)	2	3(60%)	0	40%
Stage V (n=3)	0	2(67%)	1(33%)	0

Table 3 shows that the most likely treatment outcome in patients with low-stage (stage I to II) disease had a 100% survival rate, whereas in patients with high-stage (stage III to stage V) disease, the survival rate was 44%.

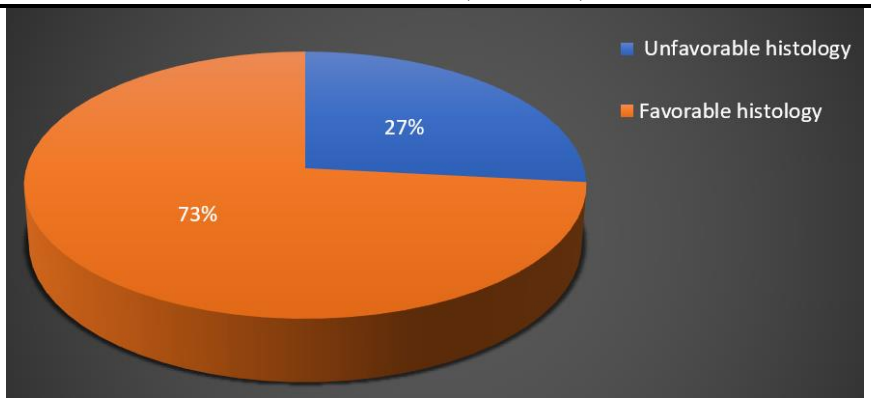

Figure 1: Distribution of Our Study Subjects by Histopathological Reports

The pie chart shows the histopathological reports of our study patients. Among 30 patients, 22(73%) patients had favorable histology, while 8(27%) patients had unfavorable histology including anaplasia. The p-value was significant (p=0.013).

DISCUSSION

The most prevalent renal malignancy in children is Wilms tumor. In Bangladesh, two distinct investigations found that Wilms tumors were more prevalent than others.[13] Locally advanced (mainly inoperable) tumors have a high incidence of micrometastasis and are more likely to rupture and spill after excision.[14] It was assumed that since chemotherapy is successful in the treatment of metastatic disease, it will also help the primary lesion to regress. The present study was done to find out the survival rate of both local and advanced Wilms tumors among children who underwent nephroureterectomy after neoadjuvant chemotherapy. This study was carried out with 30 patients of both local and advanced Wilms tumors of both sexes aged between 0 months to 6 years admitted to the Pediatric Surgery department of BSMMU.

In our study, 63% of patients were within 5 years of age and the result correlates with the previous study done by Hasina et al, where they found that 70% of patients were aged between 2 to 4 years. [2] In this study, we found a slight male predominance than females. Hasina et al also found male predominance in their study. [2] In our study, most of our patients (70%) came with anorexia, hypertension was present in 40% of patients, and abdominal pain was found in 20% of patients. Hasina et al. found anorexia/weight loss (80%), fever (60%), jaundice (60%), and abdominal pain (40%) in their study. [2]

Among our study population, 40% had low-stage (I to II) and 60% had high-stage (III, IV, and V) disease at diagnosis. Similar findings to our study were shown by Tenge et al.[15] In our study, the tumor size, depth, and volume significantly reduced after chemotherapy.

This study demonstrated a survival rate of 100% among patients diagnosed with Wilms tumor in stages I and II, and a survival rate of 44% among patients diagnosed with Wilms tumor in stages III, IV, and V. Middle-income countries have high survival rates, with China having a rate of 81%.[16] However, survival rates remain poor in low-income nations, particularly in Africa. A two-year survival rate of 25% was observed in an eight-center Wilms tumor therapeutic collaboration in Africa.[17] In Malawi, the survival rate is 46%. [18] These low survival rates have been attributed to several factors, including high treatment abandonment and treatment-related mortality.[19] In the study, we observed that patients who had stage I & II disease had good outcomes, in comparison to those who had later (lII to IV) stages of the disease. A multicenter study of Wilms tumors involving French-speaking countries in Africa reported that patients with stage III or IV disease comprised 41% of all patient cases. [20] In South Africa, those with stage III or IV disease comprised 49% of patient cases. [21]

Histological subtype also affects the outcome of Wilms tumor. In our study, 73% of patients had favorable histology while 8(27%) patients had unfavorable histology, our result is similar to the findings of a previous study. [2,22,23] This is a great improvement from the survival rate of 29% that was documented for those patients treated at the institution between the years 2000 and 2007.[24]

This study showed that the tumor found unresectable can be excised after cytoreductive chemotherapy. Therefore, preoperative chemotherapy should be given to all patients with Wilms tumor when the tumor is in an advanced stage and seems to be unresectable.

Limitations of the study

Our study was a single-center study. We took a small sample size due to our short study period. After evaluating those patients, we did not follow up with them for the long term and did not know other possible interference that may happen in the long term with these patients.

CONCLUSION AND RECOMMENDATIONS

In our study, the postoperative results were uneventful and recurrence of symptoms or any other complaints was not observed in any case. Based on the findings of the study, we observed that the earlier stage of the disease and favorable histology had a higher chance of cure compared to the late stage of the disease or unfavorable histology. We also found that advanced stage of Wilms tumor, where operative treatment was not primarily possible, preoperative chemotherapy downsized the tumor significantly. Then, it was possible to perform the nephroureterectomy on patients.

So further study with a prospective and longitudinal study design including a larger sample size needs to be done to validate the findings of our study.

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