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Wilms' Tumor Under the Control of Paediatric Surgeon

Dr. Md. Nazrul Islam[1*], Dr. Mohammad Saiful Islam[2], Dr. Md. Mahbubul Alam[3], Dr. Pravin Chaudhary[4], Dr. Muhammad Serajul Islam[5], Dr, A S M Shahidul Hossain[6], Dr. Zamil Hossain[7], Dr. Rahnuma Tasnim[8]

[1]*Consultant, Department of Paediatric Surgery, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh.*

[2]*Professor and Ex-chairman, Department of Paediatric Surgery, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh.*

[3]*Resident, Department of Paediatric Surgery, Directorate General of Health Services, Dhaka, Bangladesh.*

[4]*Resident, Department of Paediatric Surgery, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh.*

[5]*Medical officer, Department of Urology, Bangabandhu Sheikh Mujib Medical University, Bangladesh.*

[6]*Medical officer, Department of Radiology and Imaging, Bangabandhu Sheikh Mujib Medical University, Bangladesh.*

[7]*Resident, Department of Paediatric Surgery, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh.*

[8]*Medical officer, Department of Anesthesia, Analgesia and Intensive Care Medicine, Bangabandhu Sheikh Mujib Medical University, Bangladesh.*

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Corresponding Author:** ***Dr. Md. Nazrul Islam, *Consultant, Department of Paediatric Surgery, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh.*

Abstract

Background: *Wilms' tumor (WT), also known as nephroblastoma is the most common primary malignant renal tumor among children. WT is a curable pediatric malignancy; however, its management can be challenging, particularly in resource-limited settings. In this study, we aimed to determine the role of managing WT with limited resources at a tertiary care hospital.*

Methods: *This was a prospective observational study conducted in the Department of Paediatric Surgery, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh during the period from 2009 to 2019. In this study, we enrolled 30 pediatric patients diagnosed with Wilms tumor.*

Results: *The mean age of the patients was 39.5 ± 14.3 months, with a majority (63.33%) aged between 2 and 4 years. Males constituted 63.33% of the cases, and 86.66% of tumors were localized, while 13.34% were advanced. Lymph node metastases were the most common (10.00%).*

Conclusions: *Wilms' Tumor can be considered as a paradigm for multimodal and multidisciplinary treatment of malignant solid tumors in childhood. However, in developing countries, these approaches are not easily accessible and will take some time to achieve care which ultimately results in poor outcomes and increased morbidity and mortality. Hence, it is imperative to study the outcome of Wilms' tumor where the surgeon himself provides surgical care as well as chemotherapy care and thus tries to provide total care.*

Keywords: *Wilms' tumor, Chemotherapy, SIOP protocol*

1. Introduction

Wilms tumor (WT) is the most common childhood renal malignancy and the fourth most common childhood cancer.[1] Treatment of WT has been one of the great success stories of modern medicine. WT is the only childhood tumor with a good outcome (tumor-free life) if managed appropriately and on time.[2] National Wilms Tumor Study Group (NWTSG), which was supplanted by the Children's Oncology Group (COG) in 2002, the International Society of Pediatric Oncology (SIOP) has resulted in overall survival rates exceeding 90%.[2,3] Despite these remarkable outcomes, some patients have unfavorable histopathology, molecular features, bilateral involvement, and recurrent disease, which have lower survival rates.

However, in developing countries where healthcare resources are lacking as well as still in the developing stage surrounded by bureaucracy in the healthcare system, the overall survival of WT lags far behind that of developed countries.[4]

Management of WT needs a multidisciplinary approach. Surgery along with chemotherapy and radiotherapy are the main pillars. Developing countries are limited with healthcare resources (specialized hospitals, training to healthcare workers), total care planning & follow-up, and accessibility to healthcare. Apart from that not easily accessible healthcare facilities, overcrowding of patients, prolonged queues in admission/surgery or receiving chemotherapy or radiotherapy, and delayed interdepartmental referral all ultimately predisposed to increased morbidity and mortality.

In our setting, similar aforementioned problems do exist which ultimately lead to delays in getting treatment at proper time like chemotherapy. As Paediatric surgeons are the leaders in the management of WT, we share our experience of managing WT with limited resources.

Therefore, in this study, we aimed to share our experience of managing WT with limited resources and to show that WT can be managed by paediatric surgeons with limited multidisciplinary support.

2. Materials & Methods

This prospective observational was conducted in the Department of Paediatric Surgery of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh during the period from 2009 to 2019. In this study, we enrolled 35 patients with WT (unilateral/bilateral) managed at the Paediatric surgery department of our study institution. WT was diagnosed clinically and radiologically (Ultrasound of the whole abdomen and CECT abdomen).

These are the following criteria to be eligible for enrollment as our study participants:

Inclusion Criteria

a) Patients aged up to 6 years old irrespective of sex;

b) Patients with recurrent tumors.

Exclusion Criteria

a) Patients having tumors with intracaval and atrial extension;

b) Patients having non-resectable tumors;

c) Syndromic patients.

Data Collection Procedure

The aims and objectives of the study along with its procedure, outcomes, risks, and benefits were explained to the subject's legal guardian (parents) in an easily understandable language. A written informed consent was taken from patients and/or legal guardians without exploiting any of their weaknesses. This study did not cause any additional harm to the patients or animals.

SIOP Protocol

SIOP is used in managing WT. Biopsy (image-guided or Tru-cut biopsy) was only performed in special cases like situations where it is difficult to separate adrenal neuroblastoma from upper pole nephroblastoma, as an MIBG scan is not available in our setting. The Surgical Team actively participated in total care including administration of neoadjuvant (NA) chemotherapy. All patients received NA chemotherapy in a surgical care setting on a care or inpatient basis without the involvement of the medical oncology team. All presentations were subjected to NA chemotherapy except stage I. After down-staging and determination of operability [as assessed by physical examination and imaging (USG and CECT)], all underwent radical nephrectomy and histopathological staging. The chemotherapy was completed as scheduled by the SIOP protocol. Depending upon operative and histopathological findings, only a negligible number were subjected to radiotherapy.

SIOP protocol of WT [5] is given below in Table 1 & Table 2

Table 1. *Neoadjuvant Regime*

Clinical staging	Schedule
Localized	4 weeks of DAM/VCR
Metastatic	6 weeks of DAM/VCR/EPI

Table 2. *Regime of post-operative therapy as per SIOP protocol*

	Stage	Treatment
Localized	Stage I, Low grade	None
	Stage II, Intermediate grade	18 weeks DAM/VCR/EPI

	Stage II- (no lymph nodes)	28 weeks DAM/VCR/EPI
	Stage II + and III	28 weeks DAM/VCR/EPI + RT tumor bed
	High grade	34 weeks EPI/IF/VP16/CARBO + RT
Metastatic	IV	As per local stage for tumor + Treatment of metastases + RT and/or Excision

DAM- Dactinomycin; VCR- Vincristine; EPI- Epirubicin; IF- Ifosfamide; VP-16, Etoposide; CARBO-Carboplatin; RT- Radiotherapy

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 data were analyzed by using SPSS 16 (Statistical Package for Social Sciences) for Windows version 10. This study was approved by the ethical review committee of Bangabandhu Sheikh Mujib Medical University.

3. Results

A total of 35 children with Wilms tumors were enrolled in this study. Out of which, 1 died while receiving neoadjuvant chemotherapy and had a bilateral Wilms tumor. Postoperative mortality was 1 because of sepsis. 3 patients were lost in follow-up. So out of 35 WT, only 30 WT are included for statistical calculation. These 30 patients had unilateral Wilms tumors. Rights-sided Wilms tumors were 12 and left sided were 18. The overall survival rate is 85.71%.

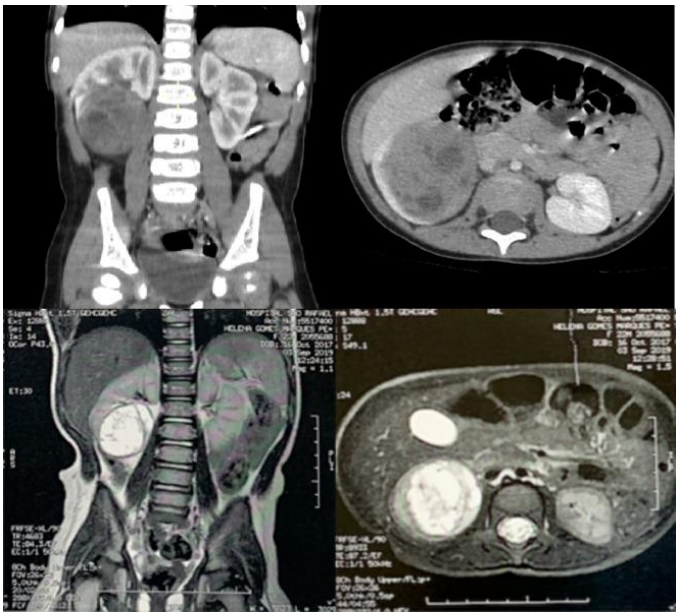

Figure 1. *Wilms tumor of a patient*

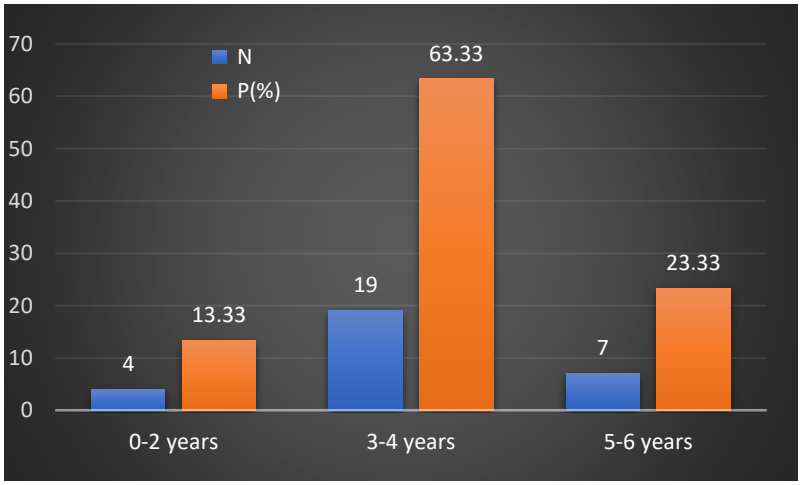

Figure 2. *Age distribution of our study patients*

Figure 2 shows the age distribution of the 30 patients diagnosed with Wilms' Tumor. The majority of the children (63.33%) were aged between 3 and 4 years. A smaller proportion (23.33%) were in the age range of 5 to 6 years, while only 13.33% were under 2 years of age.

Table 3. *Distribution of our study subjects by baseline characteristics*

Characteristics	N=30	P (%)
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	26	86.66
Advanced tumors	4	13.34
Metastases		
Lymph node	3	10.00
Lung	1	3.34

Table 3 shows that the mean age was 39.5 ± 14.3 months. The average weight of the children was 16.65 ± 4.3 kg. Males were more commonly affected, accounting for 63.33% of cases. Regarding tumor characteristics, the majority (86.66%) presented with localized tumors, while 13.34% had advanced tumors. Lymph node metastases were the most occurring in 10.00% of cases, followed by lung (3.34%).

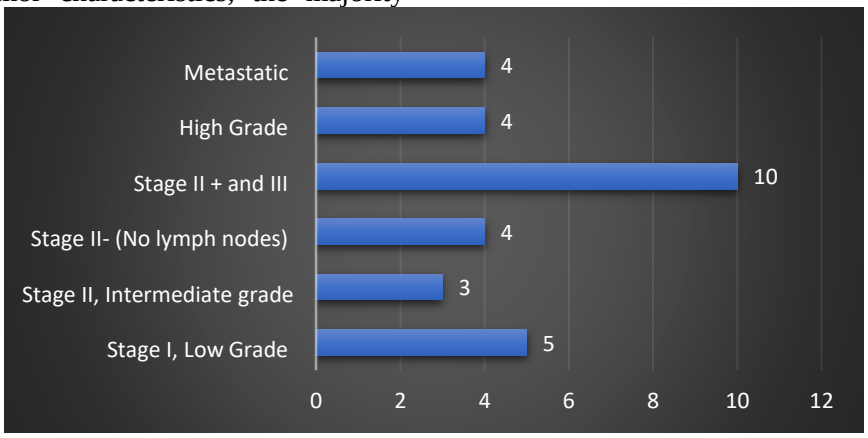

Figure 3. *Staging and distribution of Wilms' Tumor cases*

The bar chart illustrates the distribution of Wilms' Tumor cases across different stages and grades. The majority of cases (10) were categorized as Stage II and III, indicating a significant number of advanced tumors. Stage I, low-grade tumors accounted for 5 cases, while 4 cases were classified as Stage II without lymph node involvement. Another 4 cases were high-grade tumors, and 3 were Stage II, intermediate-grade tumors. Lastly, 4 cases presented with metastatic disease.

4. Discussion

Wilms' tumor was first described by Thomas F. Rance in 1814. However, Max Wilms, a German surgeon and pathologist, gave a detailed description, adding seven new patients of his own in 1899 and since then the tumor bears his name.[6] Wilms' tumor also termed as nephroblastoma is an embryonic kidney tumor. It is the most common abdominal tumor in children and represents 6% of childhood cancer.[7]

A dramatic improvement in overall survival rates lately has resulted from the coordinated use of modern surgical techniques and anesthesia, multiple-drug chemotherapy, and radiation therapy.[8] Large cooperative cancer groups, like the Société Internationale d'Oncologie Pédiatrique (SIOP) and the National Wilms' Tumor Study (NWTS) have established standards for standardized treatment of this tumor, resulting in a 5-year survival rate of over 90%. [7,8] Bilateral Wilms tumor (BWT) occurs in up to 13% of patients with WT. [9]

The median age at diagnosis is 41.5 months for males with unilateral tumors and 46.9 months for females with unilateral tumors. Most of the

patients present before 5 years of age. [10] In our study, the mean age of patients was 39.5 ± 14.3 months with male predominant and unilateral tumors. Most of the patients were below 5 years old.

WT is associated with congenital anomalies in 10% to 13% of cases like Aniridia, Hemihypertrophy, Beckwith-weidmen syndrome, renal anomalies, etc.[11] However, we did not encounter any associated anomalies in our cases.

Patients usually present with a smooth and non-tender flank mass on palpation, as noted by a parent. About a quarter may have associated (microscopic) hematuria, dysuria, malaise, weight loss, anemia, or hypertension. [12] In this study, most of the patients presented with flank mass.

Detailed preoperative imaging (Ultrasound and CT Scan or MRI) and exact renal tumor staging are important for planning the surgical approach and strategy, and for providing accurate prognostic information for the patient.[13]

On CT scans, Wilms' tumor usually appears as a large, round mass within the kidney, showing less enhancement than the surrounding normal renal parenchyma. Areas of heterogeneous attenuation can be present secondary to hemorrhage, calcification, or fat.[14] We followed SIOP protocol, so radiological investigations are given more priority especially ultrasound and CECT scans of the whole abdomen.

Even though the management of WT depends upon a multidisciplinary approach, in a developing country like Bangladesh where specialized chemotherapy or radiotherapy centers are less and are difficult to access, WT patients have to keep in the queue to get these facilities. Receiving treatment at the ideal time will improve the outcome. Surgeons being a leader and total care planners, it is their obligatory duty to make a care plan for WT patients. We started to provide chemotherapy practice in the surgery department so that a WT patient doesn't have to go chemotherapy department and does not have to wait in prolonged queues.

Suman BA found that 38% of patients have to wait in queues to get treatment in developing countries which causes delays in treatment. [15] Similarly, it is estimated the median waiting time of 18.2 weeks for a patient to get medical treatment in a developed country like Canada.[16] So, everyone can predict the waiting time in developing countries will be much longer. Murray suggested that patients experience long waiting times in the health care continuum in three major areas: first, in waiting for access to an appointment in primary care; second, in the medical office itself; and third, in waiting for access to specialty care once the primary care physician has decided to refer the patient.[17] Montero et al proclaim that the delay between admission and the request for inter-departmental consultation was 12.6 days on average and around 90% of the in-hospital consultations for patients undergoing surgery were requested after the intervention.[18]

Short-term outcomes in pediatric cancers are better than in adult cancers, but relapses are often unpredictable, and most current treatment protocols depend on cytotoxic agents with significant long-term complications.[19] However, we haven't encountered long-term complications in our WT patients.

A critical challenge in resource-limited settings is ensuring access to comprehensive care, including chemotherapy, surgery, and long-term follow-up. Pediatric surgeons in these regions often face a lack of resources, training, and multidisciplinary support, which can hinder the effective management of WT.

5. Conclusion

Often standards for care are set such that many in the underprivileged context are denied of the deserved care and achievable outcomes. With the continuous improvement in the accessibility to care settings in Developing Countries including Bangladesh, appropriate specialized care settings are often absent. The outcome of this initiative over a period of ten years invites healthcare planners, designers, and providers to rethink out of the box. The gratifying outcome indeed speaks strongly for taking the context and available resources even though short of optimum into consideration to design and deliver effective healthcare. The Experience affirms that Surgeons with orientation to and training in cross-disciplinary competencies that may expand their spectrum of total care can become the focal point of the extended care spectrum. This will certainly increase accessibility to care, facilitate recruitment of patients, and improve outcomes of conditions that are considered out of the spectrum for a particular care setting.

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