ORIGINAL ARTICLE

EARLY OUTCOMES OF WILMS TUMOUR SURGERY IN CHILDREN TREATED WITH PRE-OPERATIVE CHEMOTHERAPY: AN EXPERIENCE FROM CANCER DEDICATED CENTER

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Background: In recent times, advances in surgical technique and chemotherapy resulted survival rate in Wilms tumour patients approaching 90%. Therefore, the study aimed to assess the efficacy of preoperative chemotherapy and to document the early postoperative surgical and oncological outcomes. **Methods:** The patients with Wilms tumour who underwent radical nephrectomy from April 2020 to May 2023. Factors related to demographics, radiological findings, treatment provided, response to chemotherapy, and short-term outcomes were assessed. Mean and standard deviations were used to describe categorical data while frequencies and proportions were used to describe quantitative data. **Results:** Ninety patients with Wilms tumour received pre-operative chemotherapy and underwent radical nephrectomy with a mean age of 3.35±2.20 years. The majority of the patients presented within three months of the onset of the symptoms (81.0%) and the common symptom was abdominal mass (77.7%). Most of the patients were lying in the intermediate-risk stratification group (70.0%). The mean operative time was 2.02±0.75 hours. The mean high dependency unit (HDU) stay was 1.57±1.31 days and the mean hospital stay was 3.47±1.14 days. Furthermore, surgical complications were reported in nine (10%) patient, and four patients had early relapse, and two expired. There was a statistically significant chemotherapy response in terms of tumour size (pre-chemotherapy 9.6±3.29 cm versus post-chemotherapy tumour size 7.1±2.8 cm). **Conclusions:** Despite the delayed presentation and large volume of tumours, the initial results are favourable. Additionally, preoperative chemotherapy has played a crucial role in reducing tumour size and enabling successful surgical removal.

Keywords: Wilms Tumour; Children; Pre-operative chemotherapy; Nephrectomy

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INTRODUCTION

Wilms' tumour (nephroblastoma) is one of the most common (90%) renal tumours in children. In recent times, advances in surgical technique and chemotherapy have resulted in a great improvement in prognosis and the survival rate approaches 90%.[1,2] Surgery and chemo-radiation is the standard of therapy; however, pre-operative chemotherapy leads to a decrease in tumour size and down-staging of tumours with fewer tumour ruptures and spillage during surgery with the possible omission of postoperative irradiation. Moreover, a histologic response to therapy and tumour necrosis was used for postoperative risk stratification.[3]

John R. in their cohort reported an excellent response to preoperative chemotherapy with a reduced mean tumour size of 208 ml and resolution of venacaval thrombus.[2] While, in another study, Nyakundi *et al*, proposed the early postoperative complications with intestinal obstruction in 6.7%, surgical site infection in 3.3% and tumour rupture in 3.3% patients. Additionally, post-operative ward stay was an average of 6.5 (SD±1.6) days, with significant (p=.044) association seen between duration of symptoms and surgical ward stay.[4]

Despite advances in adjuvant therapy[5], surgery plays a critical role in the oncologic treatment of Wilms' tumour, and complete tumour resection without complication is important for post-operative staging, which ultimately directs adjuvant therapy.[3] Furthermore, precise surgical guidelines are well established and fundamental for obtaining favourable results.[6] Nonetheless, surgical complications are recognized morbidity of the treatment of patients with Wilms' tumour, and their management remains an essential part of paediatric oncological management.[5]

Late presentation, tumour burden, treatment abandonment, and limited access to oncological treatment are the major challenges found in developing countries.[7] The data is scarce regarding the standard management and surgical outcomes of children with Wilms tumours, especially from the developing world. Therefore, the purpose of this study was to assess the efficacy

of preoperative chemotherapy on tumour size, tumour resectability, rupture/spillage, and to document the early postoperative surgical and oncological outcomes.

MATERIAL AND METHODS

This was a retrospective review of prospectively maintained database of hospital, included all the paediatric patients up to 18 year of age who subjected to surgical resection from April 2020 to November 2023. Institutional Review Board (IRB = EX-23-06-23-02) approval was obtained. After initial workup and diagnosis based on imaging all the patients were managed according to SIOP-RTSG 2016 UMBRELLA protocol (International Society of Paediatric Oncology - Renal Tumour Study Group)[8] and received neoadjuvant chemotherapy, two drugs (Vincristine and Actinomycin D (AV) X4 weeks) for non-metastatic tumours and three drugs (Vincristine, Actinomycin D and doxorubicin (AVD) X6 weeks) for metastatic tumours.

Following adjuvant chemotherapy and reassessment scan, radical nephrectomy with retroperitoneal lymph node sampling was performed. Adjuvant chemo-radiation was given according to final histopathology and risk stratification. The patients with residual metastatic disease underwent metastectomy and then followed regularly in clinics. Variables including demographics, radiological findings, adjuvant chemotherapy and response to chemotherapy, surgical and histological details, peri & post-operative surgical complications, and early outcomes including duration of hospital stay, relapse and mortality with the follow up of at least 90 days were analyzed. The IBM SPSS version 20 (IBM Corp., Armonk, NY, USA) will be used for data analysis. Mean and standard deviations were used to describe categorical data like gender, tumour stage and laterality, risk stratification, while frequencies and proportions were used to describe quantitative data like age, tumour size and necrosis, peri and post-operative variables. A *p*-value of <0.05 was considered statistically significant for chemotherapy response to tumour size.

RESULTS

Ninety patients with Wilms tumour received pre-operative chemotherapy and underwent radical nephrectomy and retroperitoneal lymph node sampling. The mean age was 3.35±2.20 years with age ranged from one to seven years and majority (56.7%) were males (Table-1). Most of the patients were belonged in the intermediate-risk stratification group (70.0%) followed by (28.9%) in the high-risk group (Table-2). There was a statistically significant (*p*=.005) chemotherapy response in terms of tumour size with pre-chemotherapy tumour size of 9.6±3.29 cm versus post-chemotherapy tumour size of 7.1±2.8 cm (Figure-1). Twenty-eight (31.1%) patients had good response with more than 90 % necrosis.

Six patients had residual tumour extension into the renal vein (4) and inferior vena cava (2) and underwent tumour thrombectomy. Additionally, out of twenty-two, eight patients had residual metastatic disease and underwent second surgery (Table-3). The mean operative time was 2.0±0.75 hours. Mean blood loss was 53.8±69.1 ml. The mean high dependency unit (HDU) stay was 1.57±1.31 days and the mean hospital stay was 3.47±1.14 days. Furthermore, surgical complications like tumour spillage were reported in four patients, post-operative wound infection in two patients, adhesive bowel obstruction in two patients out of which one patient re-explored due to failure of conservative treatment. Regarding oncological outcomes, eighty-four patients had complete remission, four patients had early relapse and are under treatment, and two expired due to chemotherapy related toxicity (Table 4).

Table-1: Demographics and clinical characteristics

Characteristics	**(n= 90)**
Gender	
Male	51 (56.7%)
Female	39 (43.3%)
Clinical Presentation	
Abdominal mass	70 (70.4%)
Abdominal mass + haematuria	20 (10.4%)
Site of primary Tumour	
Right side	46 (51.1%)
Left side	43 (47.8%)
Bilateral	01 (1.1%)
Association	
Horseshoe kidney	02 (2.2%)
Cross Ectopia	01 (1.1%)
Undescended testes	03 (3.3%)

Table-2: Tumour characteristics and risk stratification

Characteristics	**(n= %)**
Stage of tumour	
I	04 (4.4%)
II	34 (37.8%)
III	29 (32.2%)
IV	22 (24.4%)
V	01 (1.1%)
Site of metastasis	(n=22)
Lung	17 (18.9%)
Lung + Liver	02 (2.2%)
Liver	03 (3.3%)
Risk stratification	
Low risk	01 (1.1%)
Intermediate risk	63 (70.0%)
High risk	26 (28.9%)

Table-3: Surgical and histological details

Characteristics	(n= %)
Radical nephrectomy	(n=90)
Tumour thrombectomy	06 (6.6%)
Renal vein	04 (4.4%)
Inferior vena cava	02 (2.2%)
Metastectomy	08 (8.8%)
Lungs (VATS)	06 (6.6%)
Liver	02 (2.2%)
Lymph node yield (mean)	5.37±3.1
Positive	03 (3.3%)
Negative	87 (96.7%)
Histological sub-types	
Epithelial type	51 (56.7%)
Stromal type	46 (51.1%)
Blastemal type	53 (58.9%)

Table-4: Surgical and oncological outcomes

Characteristics	(n= %)
Surgical Complications	09 (10%)
Tumour Spillage	04 (4.4%)
Wound infection	02 (2.2%)
Adhesive Bowel Obstruction	02 (2.2%)
Re-exploration	01 (1.1%)
Oncological outcome	
Complete remission	84 (93%)
Recurrence	04 (4.4%)
Death	02 (2.2%)

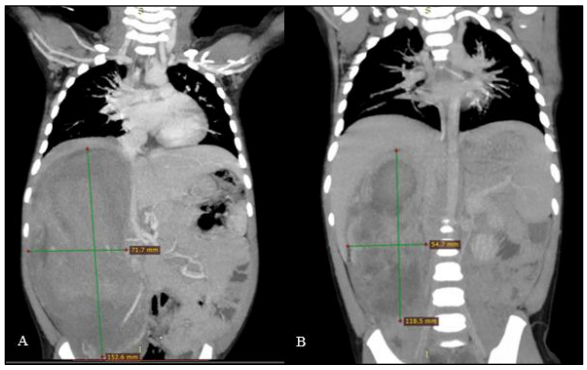

Figure-1: A: Heterogeneous right renal mass measuring 152×71.7 mm pre-chemotherapy vs B: Right renal mass measuring 118x54.7 mm post-chemotherapy with interval significant internal tumour necrosis

DISCUSSION

Wilms' Tumour (WT) is a cancer that can be cured and is reported to have excellent long-term outcomes in well-developed countries. Advances in multimodality treatment has improved survival and have aided in the reduction of morbidity from surgery.[7] Despite advances in adjuvant therapy, surgical excision of tumours and management of surgical complications remain a crucial aspect of paediatric oncological care.[9] Nevertheless, the replication of these elevated cure rates in developing nations proves elusive. Obstacles such as restricted access to oncological facilities, financial constraints, delayed diagnosis, and treatment abandonment have been previously delineated as contributory elements. Previous surgical interventions, incomplete staging assessments, and treatment abandonment emerge as recurrent obstacles.[7]

Our institution is a state-of-the-art cancer dedicated center, and we follow a multimodal approach following SIOP-RTSG 2016 Umbrella protocol in all patients with the diagnosis of Wilms Tumour (imaging and / or biopsy proven where required). The mean age of presentation in our population subset was 3.35±2.20 years with a male predominance, which is comparable to internationally published literature including Kenya[10] Malawi[11] and China[12,13]. The most common symptom reported in literature is abdominal mass (75%).[2,4,5,13] Our study results are consistent with these findings; 77.7% of children presented with abdominal mass. WT often presents as a solitary lesion, but ~7% are reported to be multifocal and 5–9% bilateral.[14–16] In our study, we had only one patient with bilateral presentation.

Studies conducted by the Society of Paediatric Oncology (SIOP) have reported a more than half mean reduction after a single cycle of chemotherapy and a further 50% reduction after the second cycle.[17] Our results align well with this showing a statistically significant reduction following chemotherapy from 9.6±3.29 cm to 7.1±2.8 cm (p=.005). Additionally, our study shows a short operative time with a mean blood loss of 53.8±69.1 ml; we also saw a mean hospital stay of 3.47±1.14 days. This short hospital stay is far less as compared to local literature, which ranges between 6 to 7 days.[17]

The incidence of surgical complications reported in the National Wilms' Tumour Study-4 in Germany is 12.6%,[18] and local literature reports 19%.[13] The outcomes from our data depict complications in twelve patients (13.3%). Of these, tumour spillages occurred in 4.4% patients, which is comparable to studies from China with a similar disease pattern (4.5%)[12] and much less than South Africa (21%)[19]. Moreover, the incidence of bowel obstruction following surgical resection of Wilms tumour is reported to range between 5–14%,[4,20,21] and our results show only in two patients 2.2 %.

The early clinical prognosis for children with Wilms' tumour has substantially improved through the integration of combined therapeutic approaches, encompassing chemotherapy, surgery, and radiotherapy.[4,17] we observed a low complication rate and 93.3% patients in complete remission and are under follow up.

CONCLUSIONS

Despite the delayed presentation, the initial results are favourable. Additionally, preoperative chemotherapy has played a crucial role in reducing tumour size and enabling successful surgical removal.

Conflict of interest:

There is no conflict of interest for any authors.

Authorship:

All authors attest that they meet the current ICMJE criteria for Authorship.

Ethical considerations:

Institutional Review Board approval has been obtained. In addition, informed consent for utilization of patient data for research and educational purposes was obtained.

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AUTHORS' CONTRIBUTION

SA, TL: Study design, conceptualization, literature search. SA, TJ: Data collection, data analysis, interpretation. SA, AMS: Write-up, proof reading. SA, MAS: Proof reading, data collection.

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