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Original article

The Patterns of Clinical Presentation, Treatment, and Survival Outcome of Wilm's Tumor: A Six-Year Retrospective Study at a Single Cancer Institute

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ABSTRACT

Background: *Wilm's tumor (WT) is recognized as the fourth most common pediatric cancer in the United States and accounts for more than 90% of all kidney malignancies identified among children. The 5-year overall survival exceeds 90% among developed countries. The objective of this study was to look at presentation and treatment patterns, as well as figure out the outcome of WT in Libya.* ***Material and method:*** *This was a retrospective cohort research conducted between July 2017 and October 2023. We have included information on basic demographic data, clinical presentation, laboratory values, radiologic evaluation, treatment protocol, and survival months.* ***Results****: There were 38 patients, female accounts for 20 (52.6%), and the median age at presentation was 38 months (IQR 18-56.25). The most frequent presentation was palpable abdominal mass, accounting for 78.9% (30 cases). The majority of cases were late presentations at either stage III or IV, 19 (50%) and 4 (10.5%), respectively. With a median follow-up duration of 15.5 months (ranging from 3 to 70 months), the overall 5-year survival rate is 94.7%. Survival rates for children who presented with stage II and stage III were 80% and 94.7%, respectively.* ***Conclusions:*** *In conclusion, in our setting, children with Wilm's tumors present late with advanced disease and large tumors. A multidisciplinary approach can reasonably improve survival rates even in late presentations and in resource-limited scenarios.*

Keywords: Childhood Cancer, Wilm's Tumor, Overall Survival, Libya

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الخلفية: يُعترف بورم ويلم كثالث أكثر سرطان شـائع للأطفال في الولايات المتحدة ويمثل أكثر من 90٪ من جميع الأورام الخبيثة في الكلى المحددة بين الأطفال. استنادًا إلى سجل السرطان التابع لمنظمة الصحة العالمية ، تحتل ليبيا أدنى معدل موحَّد حسب العمر (ASR) لأورام ويلم في إفريقيا. كان هدف هذه الدراسة هو دراسة أنماط العرض والعلاج ، بالإضافة إلى تحديد نتائج WT في ليبيا. **المواد والطرق**: كانت هذه دراسة انسجامية استقصائية أُجريت بين يوليو 2017 وأكتوبر 2023. قمنا بتضمين معلومات عن البيانات الديمغرافية الأساسية ، والعروض السريرية ، وقيم المختبرات ، والتقييم بالأشعة ، وبروتوكولات العلاج ، وشهور البقاء على قيد الحياة. كان هناك 38 مريضًا ، حسابات إناث تصل إلى 20 (52.6٪) ، وكان عُمر التقديم المتوسط 38 شهرًا (IQR 18-56.25). كان أكثر عروض التقديم شيوعًا كتلة بطنية قابلة للشعور، تصل نسبتها إلى 78.9٪ (30 حالة). كان مُعظَّلا مُغْصِّلا لغالبية حالات التقديم في مستوى III أو IV، 19 (50٪) و4 (10.5٪) على التوالي. مع فترة متابعة من 15.5 شهرًا (تتروح من 3 إلى 70 شهرًا)، نسبة بقاء خمس سنوات هى 94.7%. في الختام، يظهر الأطفال الذين يعانون من أورام ويلم بشكل متأخر مع المرض المتقدم والأورام الكبيرة. يمكن أن يحسن النهج التعددي الاختصاصات معدلات البقاء بشكل معقول حتى في الحالات المتأخرة وفي سيناريوهات ذات موارد محدودة

INTRODUCTION

Wilm's tumor (WT) is classified as the fourth most common childhood cancer in the United States and represents over 90% of all kidney malignancies(1). Nevertheless, Wilm's tumor is regarded as the second to third most prevalent cause of child cancer in the Sub-Saharan area of Africa(2). According to the World Health Organization's (WHO) cancer registry, Mali has the highest age-standardized rate (ASR) for Wilm's tumor (WT) in Africa, while Libya has the lowest ASR at 3.3 per million people (3). The median incidence of WT, considering all cases, was 7.6 with an interquartile range (IQR) of 4.9–10.9. The statistics from Libya may not accurately represent the actual occurrence of WT when compared to the reported rates in other locations (4, 5). The only report reflecting the prevalence in the eastern region of Libya by Bubtana et al, reported that WT is the fourth cause of childhood cancer, with a peak age of four mo.– 4 years (6).

The National Wilm's Tumor Study Group (NWTS)/Renal Tumor Committee of the Children's Oncology Group (COG) and the International Society of Pediatric Oncology (SIOP) laid the protocol-driven treatment plans for WT, which need for a comprehensive therapeutic approach that includes surgical intervention, chemotherapy, and/or radiation (7). The therapeutic technique varies according to the disease load, histopathology results (favorable versus unfavorable), and the presence of certain molecular alterations (8).

Our study aims to report the patterns of clinical presentation, treatment, and survival rate that come from the pediatric oncology department of the National Cancer Institute, Misurata, Libya.

METHODS

Study design, and setting

This study is a retrospective cohort analysis conducted from July 2017 to October 2023, based on the Strengthening The Reporting of Observational Studies in Epidemiology (STROBE) Statement Criteria(9). This study was approved by the Institutional Ethical Committee at the National Cancer Institute in Misurata, Libya (Ethical Approval No. 1/2023). The medical records of 469 patients were reviewed and only confirmed histology results of Wilm's tumor were included (40 cases), detailed information on basic demographic data, clinical features, laboratory values, radiologic evaluation, therapeutic method, and survival rate. Two patients were excluded, one patient presented for completion of chemotherapy and the second one had refractory Wilm's tumor post bone marrow transplant (BMT) referred for palliative care (Figure 1).

We follow the staging classification of the NWTS IV protocol, which consisted of an initial surgical intervention, subsequent histological verification of the diagnosis, and subsequent administration of radiation and chemotherapy according to the stage of the tumor. Following a successful course of therapy, follow-up appointments were scheduled every 3 months for the first 2 years and every 6 months thereafter. Each subsequent visit included a clinical examination, abdomen ultrasound, chest radiograph, and echocardiograph on an annual basis for patients who had treatment with Doxorubicin. Relapse and disease progression, defined as the emergence of additional metastatic lesions or an increase in the size of the main lesion, were classified as recurrences.

Statistical analysis

Frequencies and percentages were used for the descriptive statistics of the variables. For continuous variables, the mean and standard deviation (SD) or median and interquartile range (IQR) due to skewness of the distribution were used. A chi-square test was used to determine the association between the study variables and the post-treatment event. The Kaplan-Meier curve to determine the overall survival of all patients. The analysis conducted by Statistical Package for the Social Sciences (SPSS) 26 software from SPSS Inc.

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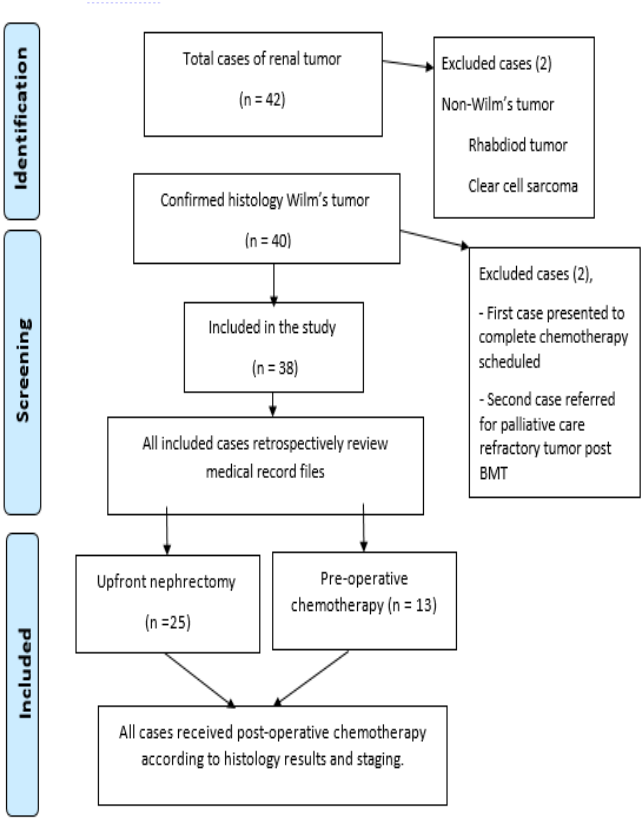

Figure 1. Flow chart for Included/Excluded Wilm's tumor cases.

RESULTS

There were 38 patients, female accounts for 20 (52.6%), and the median age at presentation was 38 months (IQR 18-56.25). Nearly 37 percent of cases (14 cases) were less than 2 years of age and 63.2% (24 cases) were above 2 years of age. The median symptom duration of 14 days (IQR 1-30 days). The median body mass index at presentation was 15.4 (IQR 13.8 – 18.1), and moderate to severe anemia was reported for 12/37 cases. The majority of cases were late presentations either stage III and IV, 19(50%) and four (10.5%) respectively. **Table 1**, Baseline characteristics of included cases.

The most frequent presentation was palpable abdominal mass accounting for 78.9% (30 cases), **Table 2** illustrates the frequency of clinical presentation. Overall, 11 (28.9%) had unfavorable histology of WT. A total of 13 (34.2%) patients received preoperative chemotherapy and all of the cases received postoperative chemotherapy and radiotherapy based on stage of disease and histopathology. Of these, one patient had lost follow-up during treatment and three cases were relapsed (7.8%). The radiotherapy timing was appropriate for 15(40.5%), delayed radiotherapy delivery for nine (24.3%), and no radiotherapy required for 13 cases.

With 37 cases available for evaluation and a median follow-up duration of 15.5 months (range, 3–70 months), the overall 5-year survival is 94.7%. The survival rates of Wilm's tumor cases according to stage and histology presented on **Table 3**. Survival in children who presented with stage II and stage III was 80%, and 94.7% respectively, **Figure 2**.

DISSCUSION

This study reports 38 patients with WT from the eastern region of Libya. WT is the commonest pediatric renal tumor, we report a female-predominant with female to male ratio of 1:0.9, as is reported in the literature (10), while others report an inverse proportion with male-predominant [1:1.05, 2:3, 1.5:1](11, 12).

Table 1. Baseline characteristic features of included cases

Features	Total patients N= 38	Frequency (%) Median (IQR)
Age	≤24 month	14(36.8)
	>24 month	24(63.2)
Gender	Male	18(47.4)
	Female	20(52.6)
Weight (Kg)	(36/38)	13.2 (9.6 – 17.75)
BMI(Kg/m²)	(36/38)	15.4 (13.8 – 18.1)
	Sever underweight (<16.5)	24(63.2)
	Underweight (16.5-18.5)	4(10.5)
	Normal (>18.5-24.9)	8(21.1)
Hemoglobin(g/dl)	(36/38)	11(9.3 – 12.4)
	Normal level (>11)	19(50)
	Mild (9.9-10.9)	5(13.2)
	Moderate (7.0-9.8)	11(28.9)
	Severe (<7.0)	1(2.6)

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WBC (×10³)	(36/38)	9.2 (6.9-12.3)
Platelet (×10³)	(36/38)	396 (280 – 491)
Stage at presentation	I	10(26.3)
	II	5(13.2)
	III	19(50)
	IV	4(10.5)
	V	-
Histology	Favorable histology	26(66.7)
	Focal anaplasia	5(12.8)
	Diffuse anaplasia	3(7.6)
	Clear cell sarcoma	1(2.6)
	Rhomboid tumor	1(2.6)
Metastasis site	Lung	4(10.5)
	Liver	2(5.2)
	Bone	-
	Brain	-

Table 2. The frequency of first clinical presentation of Wilm's tumor cases.

Clinical presentation	N (%)
Abdominal mass	30 (78.9%)
Pain	9 (23.6%)
Hematuria	3 (7.8%)
Fever	2 (5.2%)
Hypertension	7 (18.4%)
Vomiting	2 (5.2%)

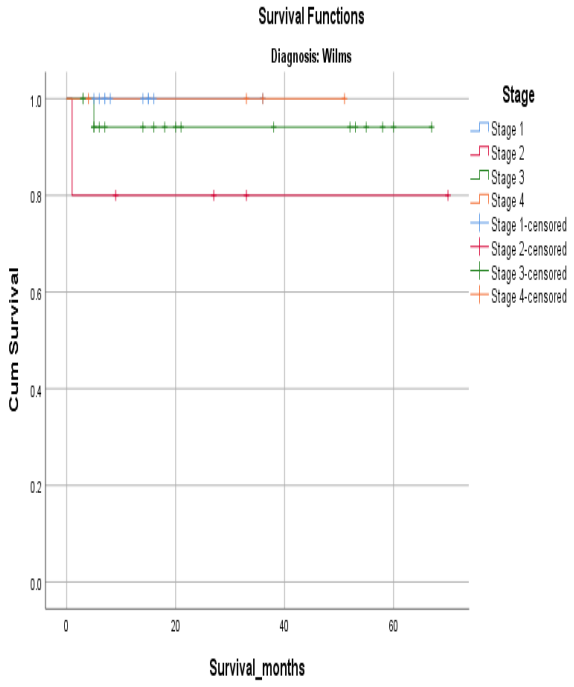

Figure 2. Estimated overall survival at 5 years was 94.7 %.

The age range of our patient's presentation were from four months to 111 months of age, which is fits with age ranges in the literature reports (6). The median age of WT was reported to be 38 months, which is similar to our report of age range (13, 14). There are literature reports an older median age of 70 months (12).

Table 3. The Survival Rates of Wilm's tumor cases according to stage and histology.

Variable	Number	EFS (%)	OS (%)
Stage			
I	10	100	100
II	5	80	80
III	18	88.9	94.5
IV	4	100	100
Total	38	92.3	94.7
Histology			
Favorable	27	92.3	96.3
Unfavorable	11	90.9	90.9
Total	38	92.3	94.7

The NWTSG Studies report a median age for females and males, of 42.5 and 36.5 respectively, which is quiet, fits with our results with median age 45 and 37 months for female and male respectively (14). In the line with the literatures 83.8% of reported cases presented above 5 years of age (6, 15).

The abdominal mass is the most common presenting symptom of WT reports(6). We have a similar report, abdominal mass accounts for 78.9% of presentations. According to the National Wilm's Tumor Study Group (NWTSG) staging, stage 3 was the most common presentation (7). The delayed presentation with advanced disease is also reported in different literature (12-14, 16).

The relapse rate in our study was 8%. The unfavorable histology accounts for approximately 33% of relapse cases. Yao et al,(17) reported a relapse rate of 4.3% for favorable, and 42% for unfavorable, while Erginel et al,(18) reported a relapse rate of 25.9% and 60% for unfavorable histology. WT survival is higher than 90% in developed countries whereas in low-income countries accounts for less than 50% (19). The

overall survival of our report is 94.7% reach developed countries. The study's limitations stem from the relatively small patient population and the inclusion of only one cancer institute. We recommend a further study that incorporates a multicenter approach and a substantial number of cases from various Libyan institutions.

CONCLUSION

In conclusion, in our setting, children with Wilm's tumors present late with advanced disease and large tumors. A multidisciplinary approach can reasonably improve survival rates even in late presentations and in resource-limited scenarios.

Conflict of Interest

The authors report no conflicts of interest.

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