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Wilms' Tumor in Children : A Single Institution 10-Year Experience

Maher K. Mustafa M , Mufeed K. Hamoury M, Salma S. Hassan R.
Pediatric Hematology/Oncology division, Queen Rania AL- Abdullah Children Hospital, King Hussein Medical Center (KHMC), Amman-Jordan.
Correspondence should be addressed to Dr. Maher Khader:
E-mail: maherrmostafa@yahoo.com , Mobile number 00962772183106

ABSTRACT

Objective: To evaluate the disease characteristics and treatment outcome of children with wilms' tumor at King Hussein Medical Center over a period of 10 years.

Methods: We conducted a retrospective review of the medical files of children (< 14 years) with wilms' tumor who were managed at King Hussein Medical Center -Jordan in the interval between June, 2000 until June, 2010 . Patients' and disease characteristics, treatment modalities and outcome were analyzed. Staging and histopathological classification were preformed according to the system of the National Wilms Tumor Study Group (NWTSG). Descriptive analysis using frequencies was used to describe the study variables.

Results: A total of 61 patients (54.1% female) with wilms' tumor with a median age of 40 months were identified. Their ages ranged between seven months and 7.8 years. The stage frequencies of our cases were : stage I (27.9 %) , stage II (34.4 %) , stage III (16.4 %) , stage IV (11.5 %) and stage V (9.8 %) . The 3- year relapse-free survival rate was 100%, 81%, 70%, 57.1% and 83.3% for stages I , II , III , IV and V, respectively. Favorable histology accounted for 86.9 % (53 cases) of our patients . The 3-year relapse-free survival rate was 84.9% for the favorable histology and 62.5% for the anaplastic histology .The 3- year relapse-free survival rate for the entire group was 82%.

Conclusion: Combined modality management including surgery , chemotherapy and radiotherapy resulted in satisfactory loco-regional and systemic control and better relapse-free survival in pediatric patients with wilms' tumor . Stage and histopathologic classification of the disease were important as prognostic factors.

Key words :wilms' tumor , Staging, histology ,Favorable ,anaplastic.

Introduction

Wilms' tumor was named after the 19th century German pathologist and surgeon Carl Max Wilhelm Wilms.[1] It originates from metanephric blastema cells that are unable to complete differentiation, resulting in triphasic tumors composed of epithelial, stromal and blastemal cells.[2]

Wilms' tumor , or nephroblastoma , is an embryonal cancer of the kidney that occurs mainly in young children.[3]It is the most common renal tumor in children and represents approximately 95% of all pediatric renal malignancies.[4,5] It is rarely found in adults with less than 1% of all WTs present in adults.[6] Nowadays, It accounts for about 6 percent of all childhood cancer cases in Europe and the United States. [5,7,8] In the United States, Wilms' tumor accounts for approximately eight cases per million children less than 15 years of age per year.[9] Wilms' tumor staging relies on two major currently used systems , the first is a postchemotherapy- based system developed by the International Society of Pediatric Oncology Renal Tumors Study Group (SIOP-RTSG) in Europe , while the second is an up-front, surgery-based system developed by the National Wilms Tumor Study Group (NWTSG, now the Renal Tumors Committee of the Children's Oncology Group) in North America. [10,11] In our institute at King Hussein Medical Center apply the frequently utilized staging system developed by the NWTSG ,which includes 5 stages and correlates with prognosis.

Histologically , Wilms' tumor is classified into anaplastic histology (AH) and favorable histology (FH). Anaplastic histology is identified by the presence of cells with nuclear enlargement, nuclear atypia and irregular mitotic figures , which can be either focal or diffuse anaplasia. The anaplastic histology accounts for

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approximately 6% of all the tumors and has adverse prognostic significance. [12]

One of the great successes in pediatric oncology is the outcome of treatment of Wilms' tumor .[10] A significant improvement in outcome from approximately 30% in the 1930s to more than 85% in the modern era has been achieved by multimodality treatment .[11] Standard treatment of Wilms' tumor in North America and most centers including our institute utilize guidelines provided by the National Wilms Tumor Study Group. It consists of upfront surgery and chemotherapy with or without radiotherapy , decided by stage and histologic classification of the tumor.[13,14]

In our study , we aimed to evaluate our institute Wilms' tumor cases regarding the disease characteristics and treatment outcome over a period of 10 years.

Methods:

This retrospective study was approved by the Ethics Committee of Jordanian Royal Medical Services. We conducted analysis of children (< 14 years) with wilms' tumor who were managed at King Hussein Medical Center in Amman-Jordan from June 2000 until June 2010 by reviewing the medical records .

Diagnosis was established by histopathology evaluation after immediate surgery for operable tumors or ultrasound-guided Tru-cut needle biopsy for inoperable tumors. Information regarding Patients' age at onset , gender , stage of disease , histopathology report confirming diagnosis , treatment modalities (surgery ,chemotherapy and radiotherapy) , re-evaluation if remission or relapse and final outcome if alive or dead were collected and analyzed .

Tumor staging ,histopathological classification and treatment guidelines followed the system of the National Wilms Tumor Study Group (NWTSG) which was incorporated into the Children's Oncology Group (COG) in 2001. Descriptive analysis using frequencies was used to describe the study variables.

Results:

We identified 61 patients who presented with wilms' tumor to our center. Thirty three (54.1%) cases were females . Their ages ranged between seven months and 7.8 years with a median age at diagnosis of 40 months. The age distribution of wilms' tumor cases showed two peaks . 68.9% of cases were observed to occur between two and 4 years as illustrated in figure 1 .

Distribution of relative frequencies of wilms' tumor stages showed that Stage I and II constituted 62.3% of all stages as illustrated in figure 2.Histopathologically, 86.9 % (53 cases) of the patients had favorable and 13.1% (8cases) had anaplastic histology as seen in table 2. The Outcome of wilms' tumor multimodality treatment in our institute was showed in table 1 and 2. The 3-year relapse-free survival rate was highest for stage I (100%) and lowest for stage IV (57.1%) .Similarly , The 3-year relapse-free survival rate was highest for the favorable histology (84.9%) and lowest for the anaplastic histology (62.5%). The overall 3-year relapse-free survival rate of the entire group was 82%.

Discussion

Jordan has a population of about 6.5 million; of whom 34.9% aged 0-14 years (Jordan Demographics Profile 2013). King Hussein Medical Center is the largest multidisciplinary medical institution in Jordan. It is one of the main referral hospitals in Jordan with a capacity of around 1100 beds. Children with cancer are referred to multiple centers including King Hussein Medical Center that has a multidisciplinary team of cancer specialists with experience of treating pediatric cancers . Jordan Cancer Registry data between January 2004 and December 2008 showed that Wilms' tumor is the sixth most common malignancy affecting Jordanian population in pediatric subgroups.

The present study showed that wilms' tumor was slightly more predominant in females (54.1%) . This result was closely comparable to an earlier Jordanian study which was conducted over a 6.5 - year period between 1992 – 1998 , and reported that out of 26 patients , 18 were females.[15] This also agrees with data from the eastern province of Saudi Arabia where the male : female (M/F) ratio was 0.8:1 .[16] In USA and Europe, a female predominance was also reported where M/F ratio was: 0.92:1 rising to 0.6:1 in bilateral cases .[17]On contrary, several studies done in Taiwan , Turkey, Egypt , Iran and Eastern China showed that the incidence of wilms' tumor was more prevalent in males.[18-22]

As illustrated in figure 1, the median age of the entire patient population in our study was 40 months which was similar to those in Egypt, Turkey, Eastern China and that of the earlier

Jordanian study ,[15,19,22,23] however, it was higher than that in Saudi Arabia where the median age at diagnosis was 30 months in a 10-year experience study.[16]

Our study described the stages of wilms' tumor in pediatric age group , as seen in figure 2. In which, the less advanced stages(stage I and II) were fortunately the predominant accounting for 27.9% and 34.4% respectively ,while stage IV constituted 11.5%. Comparing our results with the earlier Jordanian experience carried out by Haddadin et al between 1992 and 1998, we found that stage I incidence had doubled . This may indicate that the Jordanian families became more aware of the need for early medical advice to reach specialized centers for early diagnosis and treatment. Regarding the surrounding countries, earlier stages were also reported by a Saudi and Egyptian studies,[16,20] while an 18 -Year experience Turkish study reported that stage I constituted only 10% of the entire patients indicating the late presentation for diagnosis and treatment.[19] In the NWTS and SIOP, stage I accounted for 47% and 61% respectively.[24,25]

Histopathologically, 86.9 % (53 cases) of our patients had favorable and 13.1% (8cases) had anaplastic histology, whether focal or diffuse. In comparison with the earlier Jordanian data ,we found that the pattern of histopathologic findings was similar (88.5% FH and 11.5% UH).[15]This indicates that changes in the tumor pathology in not present in Jordan .These findings are close to those of the 3rd NWTS (89% FH and 11% UH), [26] the Canadian study (12.5% Anaplasia),[27] the Turkish study (88.2% FH and 11.8% UH), [19] and the Egyptian study (86.3% FH and 13.7% UH).[23]A study carried out in Saudi Arabia showed that only 6% of wilms' tumor had anaplastic type.[16] On the other hand , an Iranian study conducted between February 1992 and March 2002 revealed that 43.6% of the patients had unfavorable histology.[21] The latter was supported by a 10 years of experience at a single center in Eastern China ; in which 46 (68.7%) cases were of favorable histology and 21 (31.3%) cases were of unfavorable (anaplastic) histology. [22]This indicates the unpredictable wide variability in the histopathologic findings between the nearby countries.

In the present study, as showed in table 1 and 2, tumor relapse was seen in 18% of the entire group , highest in stage IV (42.9 %) and with unfavorable histology (37.5%) . Naguib et al reported at the National Cancer Institute (NCI) in Cairo University between January 2002 and December 2004 that The relapse rate among their patients was18.4% which lies between the rates of 17.9% and 24.2% as stated by other Egyptian studies .[23]Still our and the Egyptian relapse rate are higher than those demonstrated the 9th SIOP which was 10%. [28]

Similar to other studies, [28,29] we found that tumor stage and histopathological classification affect the life span rate. Specifically, we found that stage IV was associated with the lowest 3-year relapse-free survival rate (57.1%).Similarly, the anaplastic histology had the lowest 3-year relapse-free survival rate of 62.5% . Comparing our results with those of the Jordanian study done earlier , we can observe that improvement occurred in survival of stage IV from Zero percent before 1998 to 57.1% after the year 2000 as seen in table 1. This indicates a better management , growing experience , a multidisciplinary team approach with a wise application of combined treatment modalities (surgery, radiotherapy and chemotherapy) as well as better supportive care delivered to the patients. This study has limitations of being retrospective in nature, representing the experience of a single institution and including a relatively small number of subjects . Further larger multi-institutional prospective clinical studies are recommended to study the epidemiology and the genetic basis of this type of disease present in our region.

Conclusion

Our patients present at a median age comparable to most of the nearby and western countries. Interestingly, our patients started to contact and deal with specialized centers at earlier stages , which may indicate more awareness of Jordanian families. Furthermore, a better 3-year relapse-free survival rate of the entire group especially of stage IV compared to the earlier Jordanian study indicated the progress and improvement occurred in the applied multidisciplinary and medical care given to this type of disease. Stage and histopathologic classification were identified as independent

prognostic factors for the estimation of overall survival rate in patients with wilms' tumor.

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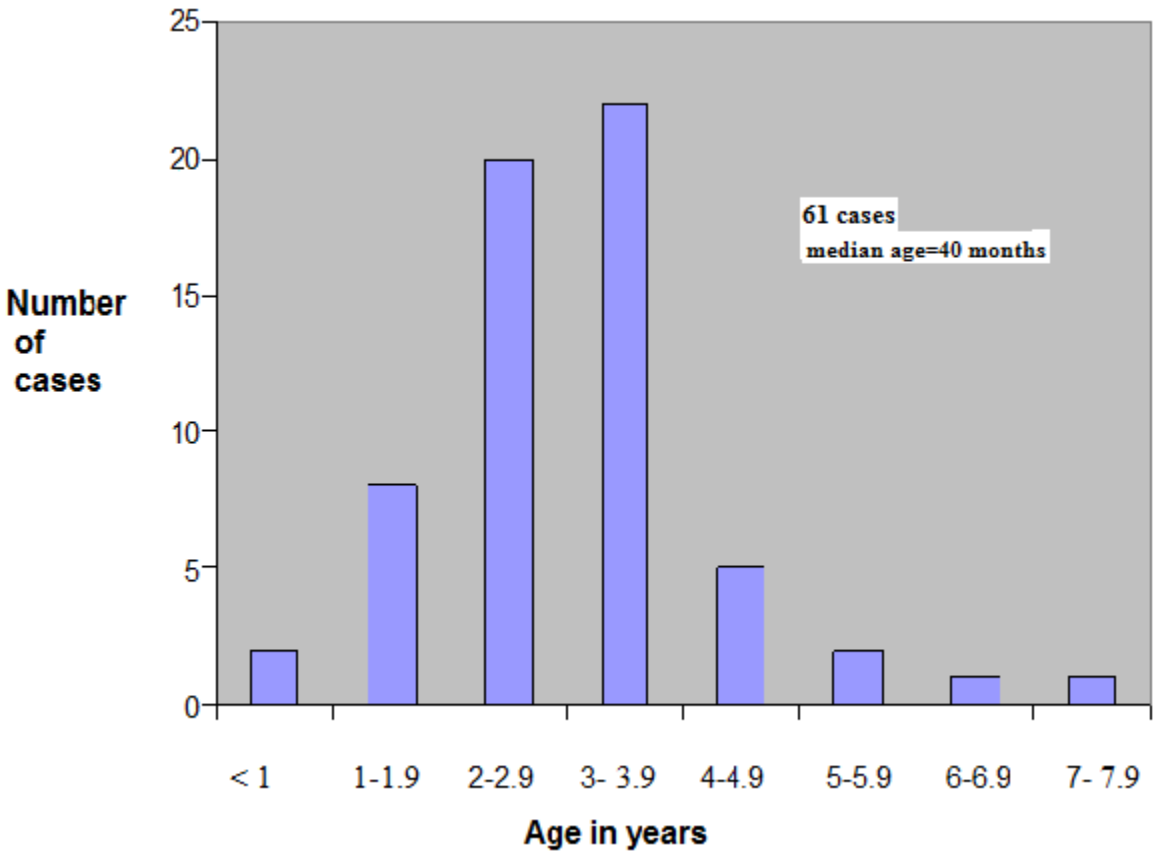

Figure 1. Age distribution of wilms' tumor derived from 61 sequential cases representing all stages . Two peaks were seen . 68.9% of cases were observed to occur between two and 4 years .The median age of all children with
wilms' tumor is 40 months and the oldest age is 7.8 years.

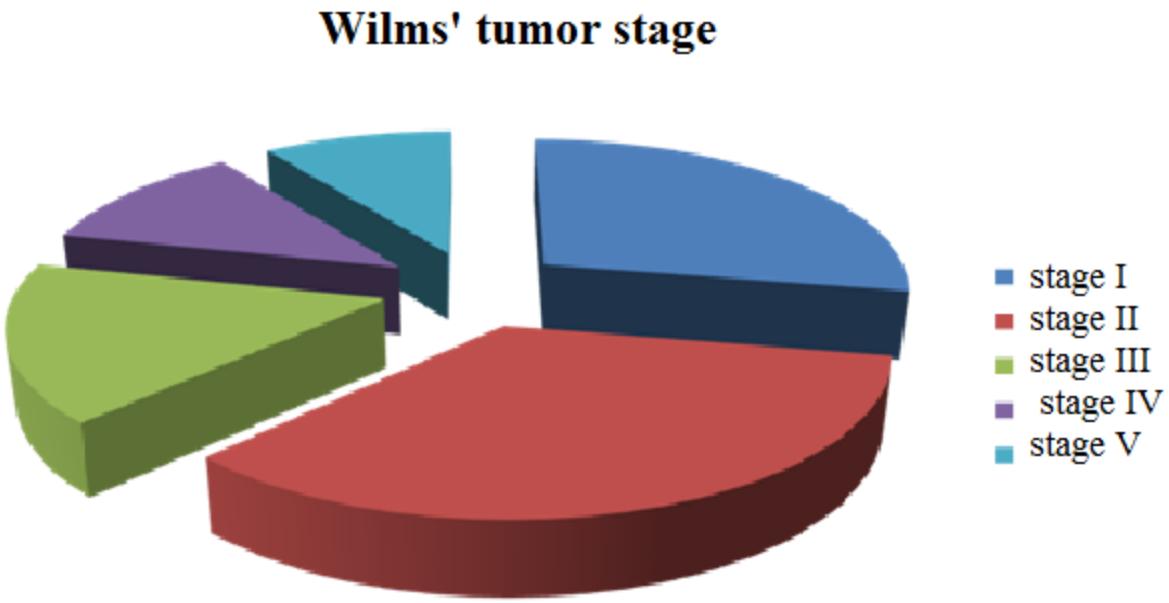

Figure 2. Distribution of wilms' tumor stages. Stage I and II account for 62.3% of all stages.

Table 1 : Outcome of wilms' tumor in relation to stage.

Stage	No. (%)	Initial treatment	Relapse No. (%)	3-year relapse-free survival No. (%)	3-year survival No. (%)
I	17 (27.9)	S,C	Zero	17 (100)	17 (100)
II	21 (34.4)	S,C ± R	4(19)	17 (81)	18(85.7)
III	10 (16.4)	S,C,R	3 (30)	7 (70)	8(80)
IV	7 (11.5)	S,C,R	3 (42.9)	4 (57.1)	4(57.1)
V	6 (9.8)	C,S	1 (16.7)	5 (83.3)	5 83.3)
All stages	61 (100)		11 (18)	50(82)	52(85.2)

S,surgery ; C,chemotherapy ; R,radiotherapy

Table 2 : Outcome of wilms' tumor in relation to histopathology

Histopathology	No. (%)	Relapse No. (%)	3-year relapse-free survival No. (%)	3-year survival No. (%)
Favorable	53 (86.9)	8 (15.1)	45 (84.9)	47 (88.7)
Anaplastic (Unfavorable)	8 (13.1)	3 (37.5)	5 (62.5)	5 (62.5)
Total	61	11	50 (82)	52 (85.2)