



PRESENTATION AND MANAGEMENT OF WILM'S TUMOUR IN SUDAN
(THREE CENTRE EXPERIENCE FROM 2014-2016)

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ABSTRACT

Background: Wilm's tumour is a cancer of the kidneys that typically occurs in children younger than fifteen year of age and rarely in adults. With an early diagnosis and proper management of wilm's tumour by Multi-modal approach excellent outcome can be obtained. This study was designed to reflect the clinical presentations and focus on different management modalities with an outcome of Wilm's tumour in Sudan.

Patients and methods: This descriptive, retro-prospective analytic study included all patients of wilm's tumour at Soba University Hospital, Gezira national paediatric surgery centre and Khartoum teaching Hospital from January 2014 to January 2016.

Results: Thirty patients (pts) were included. Females were predominant in a ratio of 3: 1 to males. The mean age was 3.0 – 5.9 years. Those who came from central and western of Sudan were more affected. Most patients presented with abdominal mass 28 pts (93.3%), followed by abdominal distension in 16 pts (53.3%), while the less frequent presentation was haematuria seen only in 2 pts (6.7%). The multimodal approach: surgery and chemotherapy used in 21 pts (70%) and single modality was used in nine patients: Surgery alone in 6 pts (20%), or chemotherapy alone in 3 pts (10%). The patients discharged uneventfully 23pts (76%). Morbidity was seen in two patients. Deaths were occurred in five patients in the study (16.7%).

Conclusion: The finding of this study reflected that Wilm's tumour has an excellent outcome when children managed by multimodal approach.

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INTRODUCTION

Wilm's tumour is a malignant tumour originating in the cells of the kidney and is most common Renal tumour that primarily affects children and rare adult ^[1], and also known as nephroblastoma. Wilm's tumour may arise in either or both kidneys. The condition is named after DR.Max Wilm's, the German surgeon in 19th century (1867–1918) who first described it.^[2] He is recognized that the cancer develops from immature kidney cells. It is made up of cells that are significantly immature and abnormal. These cells are also capable of invading nearby structures within the kidney and travelling out of the kidney into other structures. Malignant cells can even travel through the body to invade other organ systems, most commonly the lungs and brain. These features

of Wilm's tumour make it a type of cancer that, without treatment, would eventually cause death.

However, advances in medicine during the last 20 years have made Wilm's tumour a very treatable form of cancer ^[3, 4]. Treatment is a living example of success achieved through a multidisciplinary collaboration of the National Wilm's Tumour Study Group (NWTSG) and the Societe Internationale ' Oncologie Pediatrique (SIOP).^[5, 6]

PATIENTS AND METHODS

This study was conducted in Khartoum Teaching Hospital (KTH), Soba University Hospital (SUH), Gezira National centre of paediatric surgery (GNCP) in Sudan in two years' period from January 2014-January 2016. All patients in these centres were diagnosed with Wilm's tumour included. Total of thirty patients met the criterion of inclusion were studied for different clinical presentations, focusing on management modalities, duration of hospital stayed and outcome observed up to seven months.

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RESULTS

A total of 30 patients with wilm's tumour, who satisfied the inclusion criteria were studied. There is female predominant 18pts (60%) while male 12 (40%), with male to female ratio of 1:3. Most of the patients 11 (36.7%) were in the age group 3.0 – 5.9 years, whereas those more than 6 years were only 5pts (16.7%) and patients of less than one-year age were only 6pts (20%). Most of the patients were from either Central or Western part of Sudan 14pts (46.7%) and 10pts (33.3%) respectively, four patients came from East (13.3%) and only two patient from north of Sudan (6.7%).

Most of the patients presented by abdominal mass 28 (93.3%) patients and some of them associated with abdominal distension in 16 (53.3%) patients. While the less frequent symptoms over all is blood in urine seen only in 2pts (6.7%) (Table 1). Twenty-two patients (73.3%) presented in five weeks or less However 6(20%) of patients presented after the 10th week. The commonest clinical sign was abdominal mass seen in almost 29 pts (96.7%), followed by anaemia in 8pts (26.7%), while less frequent was haematuria seen in 3pts (10%),organomegaly in 4patients (13.3%) and hypertension in 01 pt. (03.3%).

Table 1 presenting symptoms of patients with wilm's tumour in the study

Symptoms	Frequency	Percent
Abdominal mass	28	93.3
Abdominal pain	07	23.3
Abdominal distension	16	53.3
Fever	09	30.0
Nausea	04	13.3
Vomiting	06	20.0
Anorexia	07	23.3
Blood in the urine	02	6.7

The investigations modalities needed to confirm the diagnosis and determine the extent and effect of the disease. Radiological investigations (Computed tomography scan and abdominal ultrasounds scan) were done in 93.3% and 73.3% respectively, laboratory investigations were done also (60%-97%), and confirmatory tissue biopsy: true cut needle biopsy (TCNB), excisional biopsy and incisional biopsy in 60 %.

There are multi-modal protocols for treatment of wilm's tumour in the study. In soba hospital the protocol of treatment is preoperative chemotherapy followed by surgery (nephrectomy), while Khartoum teaching hospital and Gezira National centre of paediatric surgery treated their patients by surgically(nephrectomy) first followed by postoperative chemotherapy. In the study multi-modal approach surgery(nephrectomy) and chemotherapy used in 21 pts (70%), while single modality was used in 9 patients: surgery(nephrectomy) alone in 6pts (20%) and chemotherapy alone in 3pts (10%). The mean duration of hospital stay was 4.0±4.2 week (range 1-15 weeks). Most of patients 22pts (73.3%) discharged within five weeks. Wilm's tumour patients who stayed in hospital four more than 10th week only 2pts (6.7%).

The majority of patients were discharged uneventfully 23pts (76%). Morbidity was seen in two patients one of chronic renal failure and other with intraabdominal haemorrhage. Deaths were occurred in five patients in the study (16.7%).The outcome was good in patients presented earlier. Patients

presented in five weeks or less, had uneventful discharge in 18/22 (81.8%) and 13.6% mortality rate, whereas those presented eleven weeks or more, had uneventful discharge in 3/6 (50%) and 33.3% mortality rate, but the difference is not statistically significant, p value 0.492. (Table2)

Table 2 Duration of the illness and outcome of treatment

Duration (weeks)	Outcome			Total
	Uneventful	Complication	Death	
1 - 5	18(81.8%)	1(04.5%)	3(13.6%)	22(100%)
6 - 10	02(100%)	0(0.0%)	0(0.0%)	02(100%)
11+	03(50.0%)	01(16.7%)	02(33.3%)	06(100%)
Total	23(76.7%)	02(06.7%)	05(16.7%)	30(100%)

P value 0.492

Twenty-one patients had multimodal treatment (surgery and chemotherapy) 18(85.7%) were discharged uneventfully, morbidity in 1(4.8%) and there were two mortalities (9.5%). Six patients underwent surgery (nephrectomy) alone: one third of them died 2pts (6%). Three patients had received chemotherapyalone: one was discharge in good condition, one develop complication and the third case died. There no relation of statistical significance found in this study between treatment modalities and outcome, p value 0.209(**Table 3**).

The follow up was short term up to ten weeks (mean; 3.4±2.7 weeks). The follow up durations in most of patients between 1-3 months 19 pts (63.3%), and less frequent follow-up period is less than one month only 1pts (3.3%).

Table 3 Modalities of treatment and outcome in patients with Wilm's tumour in the study

Outcome	Treatment			Total
	Surgery	Chemotherapy	Chemotherapy and surgery	
Uneventful	4	1	18	23
Complication	0	1	01	02
Death	2	1	02	05
Total	6	3	21	30

P value 0.209

DISCUSSION

Wilm's tumour is second common solid abdominal paediatric malignancy and the commonest type of renal tumour in children. Internationally the outcome of wilm's tumour has significantly improved in the last two decades after adopting multi-modal approach in management of the disease in most of centre. In Sudan the Wilm's tumour is also one of the most common abdominal malignancies children as showed by Hassan Ibrahim and Hatim Khalil studies^[15, 16].

In this study thirty patients whom satisfied the inclusion criteria were studied. The main age of most patients in the study was between 3.5 to 5.9 years, it. Was similar to studies done in Sudan by Abuidris DO *et al*, and Eiman Zaki Antoun.^[14,18] In Kenya the study done by Rogers T *et al* , in south Africa by Abdallah, F. K and Macharia W.M^[7,17] and internationally Green DM *et al* ^[9],all of them have similar main age to this study. In the study the female is commonly affected by disease with male to female ratio of 1:3 which is increasing than 0.9:1 reported earlier in Sudan^[8, 14, 18] and also compared to study in Pakistan by Fadoo Z *et al* revealed that male to female ratio of 1.5:1 the median age of presentation was 4 years,^[19] the reverse of this ratio is seen in Indian

studied by Green DM *et al* that showed: male to female ratio of 3:1.^[10]

Most of the patients came from centre and west of Sudan 14(46.7%), 10(33.3%) patients respectively, this was compared to Sudanese study done by Salih HM between 2006 and 2010 at Khartoum university resulted in Forty two percent of patients were from western Sudan, 4(13.3%) from east and the least from north of Sudan 2(6.7%) patients.^[8] This is similar result to two other studies done in Sudan: first by Eiman Zaki Antoun^[18], second study was done by Hassan Ibrahim on 2013 conducted in Khartoum teaching hospital and Soba university hospital^[15].

Regarding the clinical presentations most of the patients in the study presented by abdominal mass 28pts (93.3%), this is also similar to last study in Sudan done by Abuidris DO *et al* reported that abdominal mass is common presentation of the disease in Sudan^[14], also that matched with study done in south Africa by Rogers T *et al*^[7] and international by reported study by Green DM^[11]. Also most of symptoms and signs in the study were similar in both, Sudan and international comparisons^[11]. The abdominal mass associated with abdominal distension in 16 (53.3%) patients, while the abdominal Pain was the less frequent abdominal symptom seen in 7 (23.3%) of the patients, anoxia presented in only 7(23.3%)patients and the least frequent symptoms over all is blood in urine seen only in 2(6.7%) patients. In this study the most frequent duration of the symptoms was ranged from 1-5 weeks 22 (73.3%)patients and less frequent between 6-10 week only 2(6.7%) patients. From 11weeks and more 6(20%) patients presented in this period of time. Regarding duration of symptoms, I didn't find any previous studies in Sudan approved the accurate duration of the symptoms before presented to hospital.

In the study most useful tool in diagnosis of wilm's tumour is radiological Imaging: ultrasound scan was firstly described in most of patients 22(73.3%), then computed tomography scan was used in almost 28(93.3%) patients, to confirm the diagnosis and to assist evaluating the extension and invasion of wilm's tumour. In Routine investigations the most useful was the following: low haemoglobin level is noticed in 12(40%) patients while normal in 18(60%) patients, haematuria seen in only 3 pts (10%) of urine analysis, blood urea and serum creatinine were noticed to be raised in only one (3.3%) and Liver function tests was not routinely used so it was requested to only 14 patients with 3(10%)patients showed abnormality. All this data regarding the diagnostic work up were similar to international data reported by study of Green DM^[11].

Confirmatory diagnosis of Wilm's tumour after high suspicion with biopsy was remained controversial, so biopsy is used in most of the study 18 pts (60%), biopsy is taken either: TCNB which is used in 9(30%) patients, excisional biopsy in 7(23.3%) patients and incisional biopsy only used in 2(6.7%) patients. Different types of biopsy were taken according to each centre protocol: in SUH the TCNB is preferable option for diagnosis of Wilm's tumour firstly before starting the treatment, while KTH and GNCP used imaging to diagnosis before nephrectomy (excisional biopsy) was done, and all centres didn't use incisional biopsy except in inoperable cases for pathological diagnosis to start the palliative treatment. In comparison to international protocol there were two different accepted protocols regarding biopsy in patient with Wilm's tumour as follow: In North America, patients with suspected

Wilm's tumour undergo nephrectomy first. In contrast to most European centres who make a presumptive diagnosis of Wilm's tumour based on imaging findings alone. Clinicians in Europe prefer to administer chemotherapy before nephrectomy without survival compromise as seen by study of Green DM *et al*, at 1994 and 2004^[10]. Transcutaneous biopsy is not usually recommended and may in fact complicate the treatment by causing preoperative tumour spill, requiring whole abdominal radiotherapy as reported by Green DM *et al*, 1994.^[9, 10]

There were different treatment modalities in the study: surgery followed by chemotherapy was used in most of patients 21(70%), while surgery alone used in 6(20%)patients and the least used protocol is chemotherapy alone 3(10%)patients this only used in an inoperable case. So KTH and GNPC the management protocols were all for operable patients' undergoing surgery (nephrectomy) followed by postoperative chemotherapy, while in SUH they used preoperative chemotherapy followed by nephrectomy. All Sudanese centres used the biopsy then chemotherapy in inoperable cases. This match the study in Nigeria study done by Uba AF and Chirdan LB revealed that the protocol of Nephrectomy and chemotherapy were the best modality of treatments.^[20] In compared to International studied by Ruteshouser *et al* the protocol of Children's Oncology Group (COG) was usual approach is nephrectomy followed by chemotherapy, with or without postoperative radiotherapy^[13]. Also six patients in the study treated with nephrectomy alone, this met evidence suggests that certain children with stage I disease with favourable histology do well with nephrectomy alone as reported by Ruteshouser *et al*, 2008^[13].

In this study the outcome of wilm's tumour is excellent. Uneventful discharged with good outcome was seen in 18pts (60%), morbidity showed in only 2pts (6.7%) and death or unknown outcome was seen in similar number of patients in 5 pts(16.7%). Internationally approximately 80-90% of children with a diagnosis of Wilm's tumour survive with current multimodality therapy as reported in study of Pelletier J *et al*^[12]. Morbidity was seen in two patients. Deaths were occurred in five patients in the study (16.7%). Most of patients in the study continued to be followed up to first three months 19 (63.3%) patients, the least frequent follow-up period was less than one month only 1(3.3%) patients and between 4-6 months and more than 7 months had been seen in 6(20%) patients, 4(13.3%)patients respectively.

CONCLUSIONS

- WT in Sudan has similar clinical presentations compared to international reported data.
- Ultrasound scan and computed tomography were most approached tool in diagnosis of WT.
- No needed to biopsied the WT except in advanced stages of disease.
- wilm's tumour has an excellent out come when children managed by multimodal approach.
- The most used protocol in treating WT in Sudan is to do nephrectomy followed by adjuvant chemotherapy this lead to excellent outcome.

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