MANAGEMENT OUTCOME OF PEDIATRIC WILMS' TUMOR AND FACTORS AFFECTING THE OUTCOME, IN JUMC PEDIATRIC ONCOLOGY WARD, A 5 YEAR RETROSPECTIVE STUDY

THESIS SUBMITTED TO THE DEPARTMENT OF GENERAL SURGERY, SCHOOL OF MEDICINE AND HEALTH SCIENCES, JIMMA UNIVERSITY, JIMMA, IN PARTIAL FULFILMENT OF THE RE-QUIREMENTS FOR SPECIALITY CERTIFICATE IN GENERAL SURGERY

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Declaration

This is to certify that the thesis entitled‘‘Assessment of Management Outcome of Pediatric Wilms Tumor and Factors Affecting the Outcome, in JUMC Pediatric Oncology Ward, a 5 Year Retrospective Study’’, submitted in partial fulfillment of the requirements for specialty certificate in General Surgery, Jimma University, is a record of original work carried out by me and has never been submitted to this or any other institution to get any other degree or certificates. The assistance and help I received during the course of this investigation have been duly acknowledged.

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I hereby certify that I have supervised, read, and evaluated this thesis/dissertation titled ‘‘Assessment of Management Outcome of Pediatric Wilms Tumor and Factors Affecting the Outcome, in JUMC Pediatric Oncology Ward, a 5 Year Retrospective Study”, submitted in partial fulfillment of the requirements for specialty certificate in General Surgery, Jimma Institute of Health by Dr Melese Birara prepared under my guidance. I recommend the thesis to be submitted for oral defense.

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Approval Thesis for Defense Result

We hereby certify that we have examined this thesis entitled ‘‘Assessment of Management Outcome of Pediatric Wilms Tumor and Factors Affecting the Outcome, in JUMC Pediatric Oncology Ward, a 5 Year Retrospective Study’’, submitted in partial fulfillment of the requirements for specialty certificate in General Surgery by Dr Melese Birara. We recommend that ---------- is approved for specialty certificate in General Surgery.

Board of Examiners

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Abstract

Background: Like most pediatric malignancies, a survival rate of Nephroblastoma Wilms' tumor (WT) patient has noticeably improved with modern multidisciplinary cancer management. WT survival rates as reported in large trials conducted in high-income countries generally approach 90%and 70% for metastatic disease whereas in sub-Saharan Africa it is compromised by resource deficiencies with most studies reporting less than 50% survival at 5 years. This study aimed to assess theclinical outcome and different factors that influence treatment outcome of pediatric WT cases treated at Jimma University Medical Center (JUMC), Jimma, Southwest Ethiopia.

Methods: Thiswas a retrospective study. The medical records of pediatric patients aged less than 14 years who were treated for WT in JUMC from January 2017 to December 2021 were reviewed. Patient's sociodemographic, clinical, radiological, tumor histology and clinical stage, and treatment data were collected with a pretested structured questionnaire by a trained data collector. Descriptive statistical analysis and chi-square test was made with SPSS version 26. Associations were considered statistically significant with a p-value less than 0.05. The1-year survival was estimated.

Results: A total of 46 children were diagnosed with WT during the study period.Three patientswere excluded from the study because three of them didn't receive any form of therapy and had incomplete data. Forty-three patients were included in the study with median age at diagnoses was 36 months and the mean was 45.2 months (range 5–156). Twenty-eight patients were males and 15 females,and males were almost twice affected. Abdominal swelling/mass was the commonest presentation (93%).Twenty-three patients (53.5%) had locally advanced disease, 4 (7%) patients had disseminated disease to the liver and lungs and the rest had localized disease. Treatment offered was in accordance with the Societe Internationale d' Oncologie Pediatrique (SIOP) protocol; 39 were operated.Seventeen of39 operated patients had documented histologic report. All patients, except one, had favorable histology Wilms tumor.Intraoperative incidents had occurred in 5 patents. Only 16 out of 43 patients achieved complete response of the tumor after combined treatment with surgery and chemotherapy.Nine of 43patients (21%) experienced events during the study period including5 relapsesand 4deaths.The doses of chemotherapy received after surgery had statistically significant association with the OS and EFS(p=0.026). Kaplan-Meier method was applied to estimate the probability of EFS and OS.EFS was measured from date of diagnosis

of treatment failure or last follow-up and OS was measured from date of diagnosis to death and lost to follow-up. The 1-year event free and overall survival in those who took more than average cycles of chemotherapy were between 35 and 50% and between 20 and 40% respectively.

Conclusion: The main reason for poor outcome in patients with Wilms tumor was not receiving chemotherapy after surgery. Doses of chemotherapy received after surgery significantly affected treatment outcomes (p=0.026). Age at diagnosis, sex, duration of symptoms, stage at diagnosis, and the protocol used did not predict survival.

Keywords: Wilms' tumor, Nephroblastoma,Pediatric

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List of Abbreviations and Acronyms

CBC: complete blood count

CT: Computed Tomography

FNAC: fine needle aspiration cytology

G/DL gram per decilitre

HGB: haemoglobin

HIC: High income country

IVC: inferior vena cava

IVU: Intravenous urogram

JUMC: Jimma University Medical Centre

LICs: low low-income countries

LND: Lymph node dissection

LMICs: low- and middle-income countries

M/F ratio: Male to Female ratio

MRI: Magnetic Resonance Imaging

NWTSG: National Wilms tumor study group

RFT: renal function test

SIOP: International society of pediatric oncology

SPSS: statistical package for social sciences

US: Ultrasound

WT: Wilm's tumor

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1. Introduction

1.1 Background of the Study

Wilms' tumor (WT) the most common malignant neoplasm of the urinary tract of children (1), accounts for 5.9% of childhood cancers and affects one in every 10,000 children worldwide before the age of 15 years. (2)It is an embryonal neoplasm of the kidney in which blastemal, stromal and epithelial cell types are present in variable proportions [3].

Since the classical description by Wilms in 1899, the management of the tumor has evolved from surgery alone, when there were tumor rupture and peritoneal and retroperitoneal dissemination with subsequent risk of local relapse, to the multimodal treatment with surgery, chemotherapy and radiotherapy with decrease incidence of local and distant relapse [1,4].

In most high-income countries (HIC) survival rate at 5 years of more than is 90% for early disease and 70% for metastatic disease.It is due to collaboration among surgeons, paediatricians, pathologists, and institutions practicing pediatric oncology led to the formation of cooperative study groups with the aim of coordinating research on this tumor, comparing outcome of the different treatment modalities and standardizing treatment based up on risk stratification of the tumor [1, 5]. The net result of these efforts is a remarkable improvement of outcome.

The care of children with Wilm's tumor in sub-Saharan Africa is compromised by resource deficiencies that range from inadequate healthcare budgets and a paucity of appropriately trained personnel, to scarce laboratory facilities and inconsistent drug supplies making the outcome of this tumor in this setting still poor with most studies reporting less than 50% survival at 5 years. Patients face difficulties accessing healthcare, affording investigational and treatment protocols, and attending follow-ups. Children routinely present with advanced local and metastatic disease and many children cannot be offered any effective treatment. Additionally, multiple comorbidities, including malaria, tuberculosis, and HIV when added to acute on chronic malnutrition, compound treatment-related toxicities. Survival rates are poor.

Pediatric surgical oncology is not yet regarded as a health care priority by governments struggling to achieve their millennium goals. (6) Delayed diagnosis, poor compliance to treatment, and lack of multidisciplinary team for selection and stratification of patients prior to the commencement of management, which contribute to the poor outcome.

1.2 Statement of the Problem

Wilms tumor in low-income countries has survival rates of between 20% and 50%. (7-9) Reasons for the low survival is due to lack of proper care as a result of poor cancer treatment centers, shortage of trained personnel, far distances to treatment centers, and limited public transport facilities, which in turn ends up in late presentation, affecting outcomes.

Other contributors to the low survival include lack of health insurance, abandonment of treatment due to intolerable drug toxicities, nonavailability orunaffordability of the chemotherapeutic drugs, and lack of a multidisciplinary approach to the management of patients. (8,9,11)

1.3 Significance of the study

Childhood Wilms tumor is surging as an important paediatric problem in developing and sub-Saharan Africa countries. Besides these, there is a great burden of it with the disease being detected in its locally and distally advanced stages when appropriate chemotherapeutic drugs and surgical interventions will be neither available nor effective at all. Childhood solid tumors are becoming responsible for most of deaths occurring in the first fifteen years of life. Additionally, comorbidities that coexist along with the malignancy will compound treatment related toxicities which directly impairs their adherence and effectiveness of the regimen provided with it attending risk of poor survival

This study hopes to establish an understanding on the treatment challenges and outcomes Wilm's tumor at JUMC. It also gives clue about the possible adaptation or at least adoption of protocols from developed countries for the proper and consistent management of Wilm's tumor. Based on the result of the study, recommendation will be given to the clinicians working in oncology units to establish a multidisciplinary team and collaborative oncology group with other institutions for exchange of experiences on difficult to decide scenarios, for the standardization of therapy, as well as encouraging focused research in multiple institutions across the country and abroad. Furthermore, the study will benefit future researchers as an input for their subsequent reference, help them to uncover critical areas, gaps to undertake similar studies and also for the policy makers to know well about the existing problem and shape their subsequent roadmap as required.

1.4 Objectives

1.4.1 General Objectives

To assess management outcome of paediatric Wilms' Tumor and factors affecting the outcome,JUMC in the period of January 2017 through December 2021

1.4.2 Specific Objectives

To describe factors affecting the outcomes following treatment of Wilm's tumor at pediatric oncology unit, JUMC in the period of January 2017 through December 2021

To assess the outcome of Wilm's tumor treatment in pediatric oncology unit, JUMC in the period of January 2017 through December 2021

2. Literature Review

Wilms' tumor is the most common kidney tumor that accounts for 6% of infants and childhood malignancies [2, 12]. This tumor is also called nephroblastoma because of its renal origin. It can be unilateral or bilateral. Synchronous bilateral tumors have been attributed to 4.4 to 7% of cases, and asynchronous cases are accounted for 1-1.9%. The mean age of patients with unilateral Wilms' tumor is generally 44 months ,28 months in boys and 30 months in girlsand 31 months in patients with bilateral Wilms' tumor. In fact, 78% of these cases are seen in children aged 12 to 60months. The prevalence of this disease is almost identical in both sexes (male to female ratio: 0.9%) [13-14]. Approximately 10% of WT occur as part of several distinct congenital malformation syndromes.(15) Overgrowth syndromes, in particular, Beckwith-Wiedemann syndrome carry an approximately 5% risk of developing WT. (16) Syndromes involving genitourinary anomalies combined with aniridia and variable mental retardation. The most common clinical symptoms include abdominal pain, especially in cases of haemorrhage, haematuria, fever, and elevated blood pressure (25% of cases). The lung is the most common metastasis site in Wilms' tumors [17]. Furthermore, histopathology of the tumor is the most important factor in determining these patients' prognosis, where the unfavourable histopathology features are seen in only 11.5% of the patients but account for 52% of deaths (18-19).

Earlier, due to the large size of the tumor and little effort in its operation, the mortality rate was high. However, with the advancement of surgical and anaesthetic procedures, better caring for children and providing chemotherapy and radiotherapy, survival rates have increased by over 90%. There are different therapeutic protocols for children with Wilms' tumors, and the most important are the SIOP (Societe Internationale D'oncologie Pediatrique) and NWTS (National Wilms Tumor Study-4) protocols.

In Africa, with heterogeneous economic, social, and cultural endowments, there is no uniform treatment protocol for WT in the past two decades which results in variable WT outcome.This may relate to the experience of the physicians managing these cases, on the available local resources and drugs, as well as on the state of the patients at presentation. (25, 27) In the earlier decade, for undetermined reasons, NWTSG protocol was in use, while in the later decade, a trend toward increasing use of SIOP protocol is observed and still the rest use unspecified protocol.

Studies have shown that due to prevalent large size and advanced stage tumors in Africa, the SIOP protocol that stipulates preoperative chemotherapy may be invaluable in reducing

tumor volume and downstaging the disease, thereby making surgical extirpation less challenging. (29-32) The surgery-first approach advocated by NWTSG, on the other hand, may be considered in cases presenting early and with small-volume tumors. Interestingly, in addition to these two major protocols, some studies have suggested development of a different treatment protocol for African cases that will rely on risk-based classification in this setting as well as incorporate observed deficiencies in facilities, drug supply, and available supportive care to address the challenge of failure of completion of planned treatment. (1, 7, 18, 31, 33)

In the South African Children's Tumour Registry, they account for 12% of childhood cancers (44). The overall survival rate of WT in some sub-Saharan countries it is only 40% at 8 months after diagnosis (51, 52). The tumour is supposed to be more common in Africa than in Europe and the USA with a median age at diagnosis of 42 (39). The peak age is between 24 and 36 months and 75% of patients will be less than 60 months of age at diagnosis and 95% of patients will be less than 120 months of age at diagnosis. There is usually a slight female predominance (39, 41) but this is not seen in all studies (42–45).

There are very few studies from countries in Africa; one from Johannesburg showed the survival of white patients in South Africa as >90% while the black African patients did significantly worseconsidered in cases presenting early and with small-volume tumors. Interestingly, in addition to these two major protocols, some studies have suggested development of a different treatment protocol for African cases that will rely on risk-based classification in this setting as well as incorporate observed deficiencies in facilities, drug supply, and available supportive care to address the challenge of failure of completion of planned treatment. (1, 7, 18, 31, 33)

In Malawi, Wilms tumor is the second most commonly diagnosed malignant abdominal tumor after Burkitt lymphoma. (34) Survival in Europe at the time (1931–1939) when only nephrectomy was available was ~30%. (38) Overall long-term survival is now 85–90% in Europe and the USA. (36) The treatment is multidisciplinary and consists of a combination of chemotherapy, surgery and, in selected cases, radiotherapy. However, 80% of the children worldwide with cancer live in developing countries. (37) Survival of cancer in many resource-limited places is poor for a variety of reasons. Access to health care is often difficult and far from home. Patients may present late or remain undiagnosed. In the treatment centres, diagnostic and therapeutic facilities, including supportive care are usually limited. Treatment related mortality is often higher than in developed centres, especially if inappropriately toxic

regimens are given. Another common cause of treatment failure is abandonment of treatment. (36,38) Reported survival rates for patients with a Wilms tumor in Africa range between 11% (Sudan) and 70% within the collaborative network of the French-African Pediatric Oncology Group (GFAOP). (38-39) Laméris et al. 10 found, in a retrospective study of children with Wilms tumor in Malawi from 2002 to 2005, a survival of 20–50%, with 30% of patients lost to follow-up.

In Europe, preoperative chemotherapy is given to shrink the tumor, reduce the risk of surgical complications, such as tumor rupture during surgery, and induce a more favourable tumor stage at the time of surgery. (34, 41-43) This allows for a less intensive postoperative chemotherapy schedule with fewer patients requiring irradiation. This is a logical strategy for patients in developing countries where tumors at presentation are often large, supportive care limited and radiotherapy not often available. Adoption of SIOP protocol has helped Malawi to down stage the tumor and decrease the requirement of postoperative radiation which is not widely available.

In the South African Children's Tumour Registry, they account for 12% of childhood cancers [45]. The overall survival rate of WT in some sub-Saharan countries it is only 40% at 8 months after diagnosis [46-47]. The tumour is supposed to be more common in Africa than in Europe and the USA with a median age at diagnosis of 42 [44]. The peak age is between 24 and 36 months and 75% of patients will be less than 60 months of age at diagnosis and 95% of patients will be less than 120 months of age at diagnosis. There is usually a slight female predominance [44, 46] but this is not seen in all studies [47–50].

There are very few studies from countries in Africa; one from Johannesburg showed the survival of white patients in South Africa as >90% while the black African patients did significantly worse with a survival rate of approximately 65% [51]. This study also showed that the stage 4 patients had a survival rate of <50% while stage 1 and 2 patients had rates that approximated 90%.

Abandonment of WT treatment and loss to follow up after completion of therapy are common problems in sub-Saharan Africa, including Kenya, and contribute to a dismal overall survival, which otherwise exceeds 90% at five years in developed nations. (47-49) In order to develop an effective intervention to improve survival in this at-risk population, it was important to understand the outcomes of these patients with WT who abandoned care and the etiologies unique to this patient population having chosen to terminate curative treatment and routine

follow-up. Misunderstanding of non-standardized WT treatment plans, financial barriers, inefficient services, and drug shortages were the most prevalent etiologies of treatment abandonment. Parents also expressed frustration with the lack of affordable and available drugs and the other costs involved with treatment and off-therapy follow up.Abandonment of care, in addition to on-therapy mortality, remain a significant problem contributing to increased mortality from WT in Kenya and other developing countries. (50)

3.Conceptual Framework

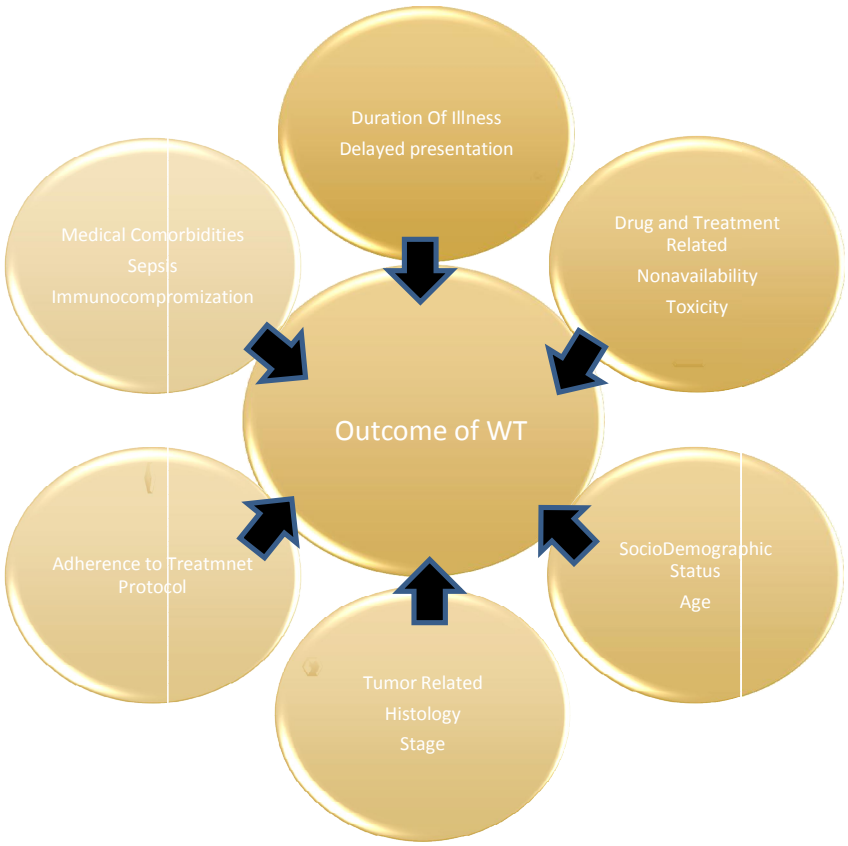


Figure 1: Conceptual Framework

4. Methods and Materials

4.1 Study Area and Study Period

The study will be conducted at Jimma University Medical Centre (JUMC), which is one of the oldest public hospitals in the country with a bed capacity of 800. Geographically, it is located in the city of Jimma, 352 km southwest of Addis Ababa. Currently it is the only teaching and referral hospital in the southwestern part of the country, providing services for approximately 16,000 inpatient, 220,000 outpatient attendants, 12,000 emergency cases in a year coming to the hospital from the catchment population of about 15 million people from southwest part of Oromia, SNNPS and Gambella regions, and from different geographical locations surrounding it, on an inpatient and outpatient treatment. It is also a training center for undergraduate and postgraduate programmes in different clinical medicine fields. Twenty beds are allocated for pediatric cancer patients. One paediatrician is involved in the care of oncology patients.Two pediatric surgeons are involved in the surgical aspect of care. There was no radiotherapy facility in JUMC until October 2021.

4.2 Study Design and Period

Facility based retrospective cross-sectional study;the study will be conducted from January 2017 through December 2021.

4.3 Source population

All children admittedto JUMC, pediatric oncology unit, from January 2017 through December 2021 will be the source population

4.4 Study Population with Eligibility Criteria

All patients with Wilm's tumour who were admitted to JUMC from January 2017 to December 2021

4.5 Inclusion and Exclusion Criteria

4.5.1 Inclusion

All patients aged less than 14 years, with confirmed Wilm's tumor who were admitted to pediatric oncology ward in JUMC from January 2017 through December 2021

4.5.2 Exclusion

All patients who had lost their cards or having a card with missed data.

4.6 Sample Size Determination and Procedure

There is no need for sampling because all patients were included in the study.

4.7 Data Collection Techniques and Data Quality Assurance

Data collection wasmade by trained data collectors using questionnaires from the medical records of each patient.

Patient's sociodemographic, clinical, radiological, tumor histology and clinical stage, and details of treatment were recorded

The completeness and consistency of the data was checked by the records made in paediatric oncology ward during data collection by the principal investigator. Whenever there appears incompleteness and ambiguity of recording the filled information formats were cross checked with the source data soon. Individual records with incomplete data were excluded. Data entry was done by standardized and consistent procedure with clear instructions to ensure data quality.

4.8 Analysis of Data

Descriptivestatistical analysis includingfrequency calculation for categorical data, and mean, median and mode for continuous data was used.A chi-square test was used to test the independence between categorical variables of interest.The results arepresented in the form of tables and text using frequency and summary statistics. Independent variable having a p value of less than 0.05 in the analytical statistics are considered to have a significant association to the outcome.SPSS version 26 was used for data entry and analysis.

4.9 Ethical consideration

Permission and approval letter from the Ethical Review Committee of the College of Medicine and Health Science was obtained prior to the study. The Research was conducted in accordance with World Medical Association Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects. Adopted by the 18th WMA General Assembly, Helsinki, Finland, June 1964.Patients' privacy and confidentiality were kept during the study time. The well-being of the individual research subject took precedence over all other interests. No informed consent was sought for this study.

4.10 Dissemination of the Result

After completing the study, the results were presented to the department of surgery. Subsequently attempts will be made to present it on scientific conferences and publish it on scientific journals.

5. Result

5.1 DemographicCharacteristics of the Patients

A total of 46 patients were diagnosed with Wilms' tumor between January 2017 until December 2021, 3 cases were excluded from the study because three of them didn't receive any form of therapy. Out of the 43 patients, 28 (65.1%)were male, and 15 (34.9%) were female with a male to female ratio of1.8:1. Theoverall median age at time of diagnosis was 36 months and the mean was 45.2 months (range: 5-156months).The peak age was between 24 and 48 months75% of patients are below the age of 60 months. The average number of cases per year was 9.6.

Table 1 Patients Demographic Characteristics

Demographics	Frequency	Percentage
Age in years		
≤1 year	7	16.3
>1-5 years	6	60.5
>5 years	10	23.3
Gender		
Male	28	34.9
Female	15	65.1
Location		
Urban	9	20.9
Rural	34	79.1

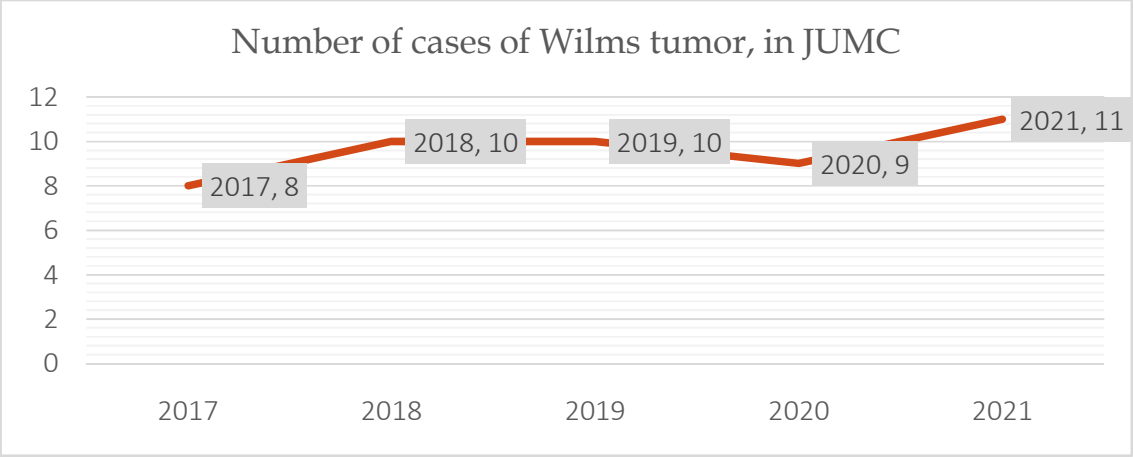


Figure 3 Number of cases of Wilms tumor, in JUMC, Jimma southwest Ethiopia, 2017 through 2021

5.2 Clinical Characteristics of the Patients

The most frequent presentation was painless abdominal swelling in 40 (93%) patients. Painful abdominal swelling occurred in 3(7%) patients. Gross hematuria, weight loss and cough were the other less frequent additional symptoms, besides the chief complaint, occurring in only 3(6.9%) patients. The medianduration of presenting complaints was 1 month (range 0.06-30months). Seventy five percent of patients presented within2 months of their symptoms and 8(18%) patients presented after 3 months of their illness.

The nutritional status was judged with anthropometry, 13 (30.2%) patients were malnourished and 30 (69.8%) were having normal anthropometry.

Fourteen patients (32.6%) were hypertensive at the time of diagnosis and the other 13(30.2%) were having normal. On abdominal examination 31 (72.1%) patients had abdominal mass not crossing the midline and 12 (27.9%) had mass crossing the midline. Associated anomalies were noted in 6 patients, including a case of isolated hemihypertrophy on the right side, a case of anophthalmia, a case of undescended testes with microphallus, a case of hypospadiasand 2cases of umbilical and inguinal hernia.

Table 2 Clinical Characteristics

Variables	Frequency	Percentage
Presenting Symptoms		
Abdominal swelling	40	93
Abdominal Pain	3	7
Additional Symptom		
Haematuria	1	2.3
Weight Loss	1	2.3
Cough	1	2.3
Blood Pressure		
Normal	13	30.2
Hypertensive	14	32.6
Not Documented	16	37.2
Abdominal Findings		
Palpable mass		
Not crossing the midline	31	72.1
Crossing the midline	12	27.9
Anthropometry		
MAM	2	4.6
SAM	10	23.3
Normal	31	72.1
Congenital Malformations		
Isolated hemihypertrophy	1	2.3
Others		
Anophthalmia plus BLUDT	1	2.3
Hypospadias	1	2.3
Hernia	2	4.6

5.3 Laboratory and Imaging Characteristics of the Patients

Hemoglobin, platelet count and renal function were assessed at admission,27 (62.8%) were anemic and 21 (48.8%) had thrombocytosis and all had normal renal function testing.All patients had undergone imaging with either USor CT scan of the abdomen. Among this ultrasound alone was done for 16(37.2%) patient and CT alone for 4(9.3%) patients and both US and CT scan for 23(53.5%) patients. Sixteen(37.2%) patients had right sided tumor and 27(62.8%) patients had left side tumor and no cases of bilateral disease or WT in a solitary kidney. Themean size was 13.8cm (Range 7.4-21cm) and two (4.3%) patients were diagnosed

to have liver secondaries.Chest x-ray was performed for all patients before the commencement of the treatment and lung metastases was diagnosed in one (2.3%)patient.Seventeen patients (39.5%) had localized disease (Stage I) and 23 (53.5%) had locally advanced tumor (Stage II & III) with the rest 3(7%) having metastatic disease to liver and lungs (Stage IV)

Table 3 Laboratory and Radiologic Characteristics of Patients with WT

Variables	Frequency	Percentage
CBC: Normal Haemoglobin	16	37.2
Anaemic	27	62.8
Normal Platelet Count	22	51.2
Thrombocytosis	21	48.8
U/A: Haematuria		
Positive	4	9.3
Negative	19	44.2
Not Documented	20	46.5
U/A: Proteinuria		
Positive	5	11.6
Negative	18	41.9
Not Documented	20	46.5
Creatinine: Normal	43	100
Abdominal US	16	37.2
Abdominal CECT	4	9.3
Abdominal US +CECT	23	53.5
CXR	43	100
Chest CT	0	0
Tumor Size		
5-10cm	8	18.6
10-15cm	20	46.5
15-20cm	14	32.6
>20	1	2.3
Tumor Laterality		
Right	16	37.2
Left	27	62.8
Bilateral/Solitary Kidney	0	0
Venous thrombus		
Renal Vein	1	2.3
IVC to the hepatic veins	1	2.3
Metastatic Site		
Liver	2	4.6
Lung	1	2.3
Stage at Diagnosis		
Localized	17	39.5
Locally advanced	23	53.5
Distant Disease	3	7

5.4 Treatmentprovided and pathologic findings

Treatment was offered for all patients in accordance with the Societe Internationale d' Oncologie Pediatrique (SIOP) protocol. Preoperativechemotherapy with regimen containing VCR+ACT-D was given for 20 patients and VCR+ACT-D+DOX for 23 patients. Forty (93%) patients received four or more weeks of preoperative chemotherapy and a median of 6 weeks postoperative chemotherapy. The resection rate was 100% for those with a unilateral tumor. The spillage rate was 2.5 %.Vinblastine was given in place of vincristine for four patients and doxorubicin was given for three patients in place of D-actinomycin and vincristine and D-actinomycin doses were missed for six patients without replacement. Thirty-nine of 43 patients underwent surgery; nephroureterectomy with LN sampling was done for 32(82%) patients and without LN sampling for 7(18%) patients. There were 5 reports of intraoperative incidents including cases of IVC and diaphragmatic injury, which were repaired immediately with uncomplicated postoperative courses, one case with tumor spillage which was limited to the retroperitoneum, one intraoperative death and a case of aortic injury which was repaired but the patient stayed in the ICU in a vegetative state for more than 70 days and the family took him against medical advice. Four patients were not operated after taking courses of preoperative chemotherapy, 3 of them were due to treatment abandonment and another had metastatic disease to the liver, died before surgery after receiving eight cycles of preop chemotherapy due to tumor progression.

Among the operated patients,33patientscame back for postoperative chemotherapy;50% of them took more than 10 cycles (more than average) of postoperative chemotherapy. Six patients didn't receive postoperative chemotherapy 3of them were due to treatment abandonment, 3 were due to death. One patient was referred for radiotherapy the rest didn't receive radiotherapy.

Table 4 Treatment Protocols and Histologic reports

Variables	Frequency	Percentage
Protocols Used (n=43)		
SIOP	43	100
NWTSG	0	0
PreopChemoRegimen		
VCR+ACT-D	20	46.5
VCR+ACT-D+DOX	23	53.5
Postop Chemotherapy(n=30)		
VCR+ACT-D	5	16.6
VCR+ACT-D+DOX	28	83.3
Type of Surgery (n=39)		
RNU+LNS	32	82
RNU alone	7	18
Non-Operated	4	10
Histology Subtypes (N=17)		
Unfavorable	1	5.8
Favorable	16	94.2
Nodal Status (N=12)		
Positive	6	50
Negative	6	50

5.5 Follow-up and Outcomes

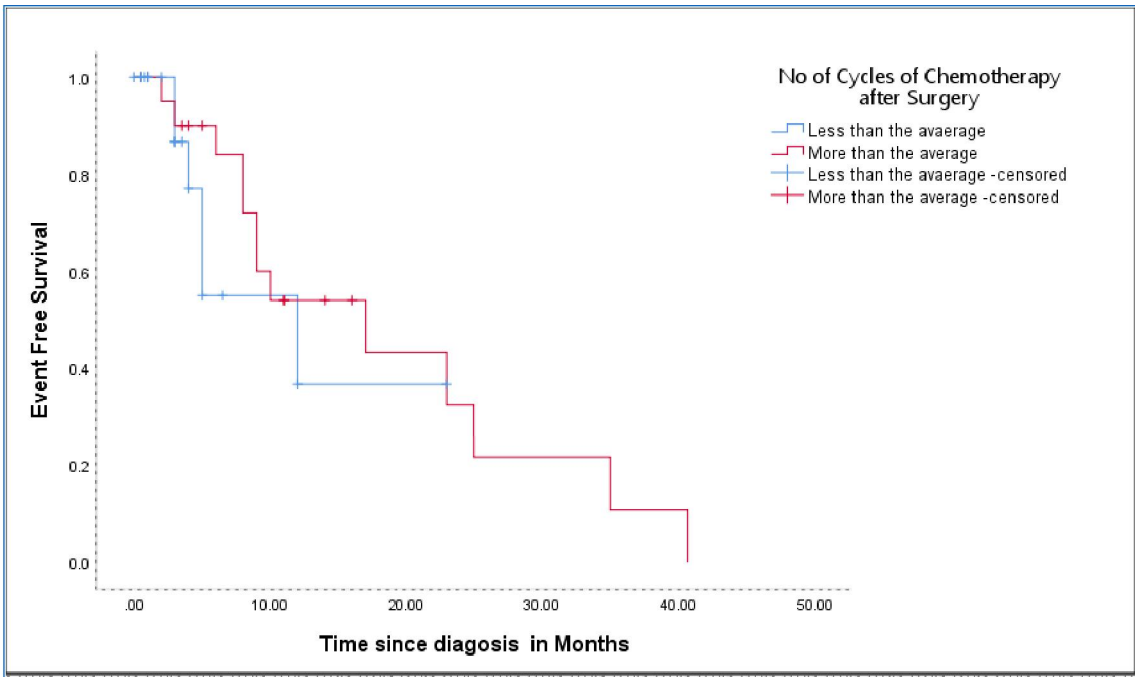
Length of follow-up varied from 0.5 to 40 months with a mean of 8.4 months. Totally, from 43 patients 16 (37.2%) patients had clinical improvement,18 (41.8 %) patients abandoned their treatment. Five (11.6%) tumor recurrences and 4 (9.3%) deaths had occurred. One patient died while being operated due to cardiac arrest and the other 3 died due to the tumor itself.

From those who were clinically improved, 50% of them were on follow up for more than 6 months from diagnosis. All deaths occurred within 4 months of diagnosis. Treatment abandonment rate is 41.8% but no reason was found.

Events that were used to measure survival were death, recurrence and lost to follow-up. The 1-year event free and overall survival in those who took more than average cycles of chemotherapy were between 35 and 50% and between 20 and 40% respectively.

Table 5 Outcomes of WT management at JUMC, Jimma (2017-2021)

Outcomes	Frequency	Percentage
Clinically Improved	16	37.2
Relapses	5	11.6
Treatment abandonment	18	41.8
Death	4	9.3



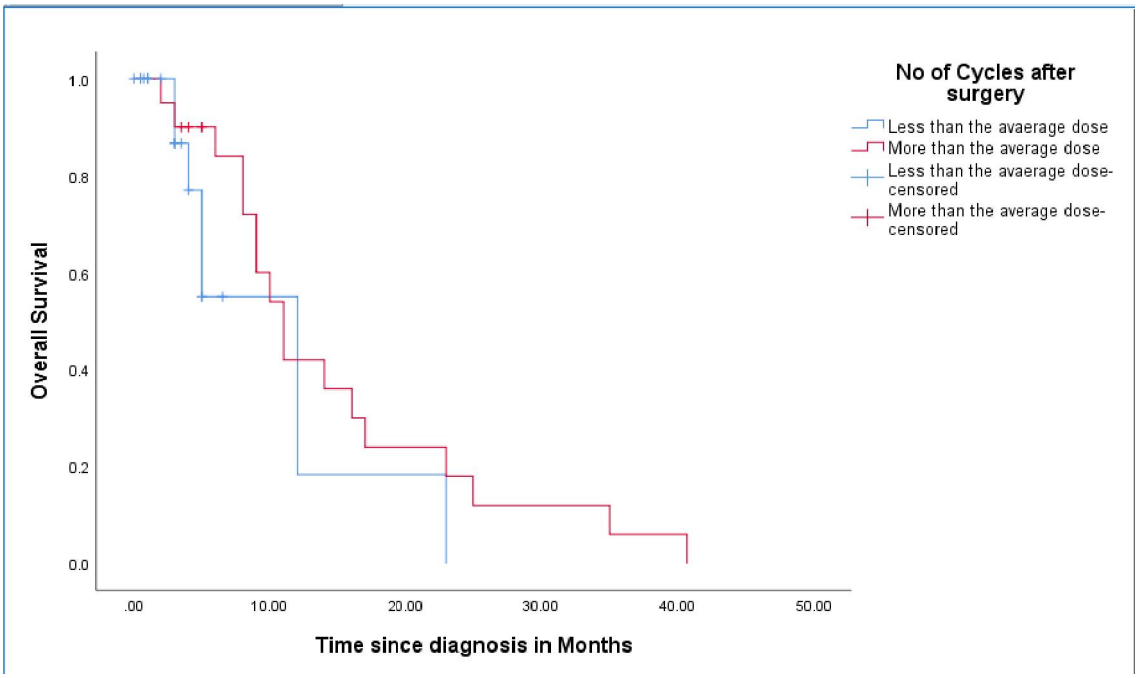


Figure 4 Event Free Survival and Overall Survival of patients with Wilms tumor treated at JUMC.Jimma Southwest Ethiopia 2017-2021

6.Discussion

There are no data on the incidence of WT and other solid tumors in Ethiopia. The frequency of childhood cancer is alarmingly increasing over years. It could be due to the increased public awareness and the health seeking behavior of the community. Wilms tumor is the second most common solid tumor of childhood. (66)

Total of 43 patients were diagnosed with Wilms tumor in the 5 five years study period giving an average of 8.6 new cases each year. The female to male ratio was 1.8 to 1. This finding was congruent with the findings of a study conducted in Gondar and Turkey where, where there was a male to female ratio of 1.6 to 1 and 1.35 to 1 respectively. (21,66) There was a slight female predominance in in the USA and South Africa. (21,44) Thisfinding was also found to be different from other studies performed in Europe and Taiwan where the male to female ratio is equal. (21,58)

The mean age at diagnosis was 45.2-months (median 36-month, range 5 to 156-months),75% of the patients were younger than 60-months old, then after the incidence steadily decrease with age. These findings were close to the findings of a study in Nicaragua, where the median age at diagnosis was 36 months (range 9.6–96 months) and in Malawi, where the mean age at diagnosis was 50.4 months (range 10-158.4 months). (20,32) This was a tumor of younger age and other studies conducted in Taiwan had shown similar results. (58) Another study, conducted in Rwanda, where a different result was found, the median age at diagnosis was 96 months (range12-120 months). (71)

Forty of 43 patientspresented with abdominalmassand 3 were with abdominal pain. This finding was comparable to other studies in Africa and other parts of the world, where majority of patients presented with abdominal swelling. (45)The other additionalcomplaints were, hematuria, cough and weight loss, each accounting for 2.3%. A study conducted in Southern Taiwan showed that abdominal mass and distension was the most frequent complaint accounting for 47.1% and 35.3% respectively. Abdominal pain was uncommon presentation accounting for 5.9 cases, but hematuria was recorded in 32.4% patients. (54)Abdominal mass and pain were the most common presenting symptom because it was the easiest noticeable symptom by the family. (55)

Patients had symptoms for a median duration of 1 month(range 0.06-30monthss) at presentation. Congenital anomalies were found in 5 of 43 patients with Wilms tumor. This finding was comparable to the studies conducted in Southern Thailand where associated

anomalies, including a case of aniridia, a case of albinism and a case that had penoscrotal hypospadias with unilateral undescended testes were found in 8.8% of the patients (54) This finding was also comparable to a turkey study where associated malformations including cases of macroglossia, hypospadias and aniridia were found in 2.8% of the patients. (21)

All patients had unilateral tumor. The left kidney was more frequently involved than the right, with 27 (62.8%) being on the left and 16 (37.2%) tumors were right sided. This finding was similar to the studies in Kenya where the left kidney was affected in 56%. (52)This finding was also similar to that of Southern Thailand and Rwanda where the left, the right and both kidneys were involved in 50% and 63.2%, 44.1% and31.6 and 5.9% and 5.2% of cases respectively. (54,71) In other studies, conducted in Malawi and Turkey, the right kidney was affected in 55% of the cases. (52-54)

The average size of the tumor by imaging is 13.8cm with a median of 13.5±3.5cm (range 7cm to 21cm) and mode of 15cm. Three-fourth of the tumors were larger than 16cm. These findings were in contrary to findings of Tang F, Zhang H and et al finding in which laterality is almost proportional and majority of tumors were less than 7cm. (67)

Seventeen (39.5%) patients hadlocalized WT, 23(53.5%) had locally advanced and 3(7%) and no cases of bilateral tumor or a tumor in a solitary kidney. had distant disease which meant majority of the patients whom came to JUMC resented with advanced disease. The finding was comparable with findings in Egypt, where 57.1% of the cases presented with locally advanced (stage II and III),21.4% with localized disease, 15.5% and 5.7% disease with stage IV and V disease, respectively. (23)A study conducted in Nigeria72% were stage III and IV and in Sudan 78% were stage III and IV. Also, in Malawi,the stages of disease at presentation werelocalized in 24% of the cases and 76% locally advanced in 76% of the cases. (32)this finding was also comparable to the study conducted in Rwanda where majority (65%) of patients presented with locally advanced (stage II & III) disease. (71)

Histologic report after nephrectomy was documented only for 17 patients.Most of the patientshad favorable histology in16(94%) patients and unfavorable histology with diffuse anaplasia in 1 (6%) patient.This finding was comparable tothe findings of a study conducted in Tanzania where 90% and 10% distribution of favorable and unfavorable histologies were reported respectively. (68) but in case of Egypt the unfavorable histology was a bit higher (33%) as compared to our finding and that of Tanzania. (23)

Length of follow-up ranged from 0.5 to 40 months with a mean of 8.4 months. Median follow-up time is almost 4 months (mean ± SD=7±8.4 months).This was shorter than the findings in Nigeria where the mean follow-up duration was 23 months (range, 6–80 months).(24) Eighteenpatients abandoned their treatment and half of them did within 4 months of diagnosis. Treatment abandonment rate was41.8%. Treatment abandonment rate is 41.8% but the root cause for abandonment of treatment were not clearly documented need further research. This finding was comparable to a study made in Kenya where the treatment abandonment rate was 50%. (69,72)

Demographic profile, clinical characteristics of patients and stage and histology of the tumor did not have statistically significant impact on survival.

No statistically significant relationship with outcome was found for gender (P = 0.581), duration of illness (p=0.208), tumor size (p=0.49), nodal status (P = 0.521), stage at presentation (p=0.764) and the protocol used (p=0.476). The statistically significant variable which positively influenced the outcome was the number of post-operative chemotherapy doses received (p=0.026). This finding was in contrary to the findings of other studies conducted in majority of African countries, in which disease stage at presentation and tumor volume were prognostically more important. The type of protocol used didn't affect the EFS or the OS of patients with Wilms' tumor but the postoperative dose of chemotherapy did (p=0.026).Kaplan-Meier method was applied to estimate the probability of EFS and OS.EFS was measured from date of diagnosis of treatment failure or last follow-up and OS was measured from date of diagnosis to death and lost to follow-up. The 1-year event free and overall survival in those who took more than average cycles of chemotherapywerebetween 35 and 50% andbetween 20 and 40% respectively. These findings were similar to other African studieswhere the 8- months overall survival was nearly 40%, except in Sudan where their OS was 11%, but still it was less than that of western countries where survival is greater than 90%. (36,38,39,46-47). Survival in Europe during 1930s, when only nephrectomy was available as at treatment option for WT, was ~30%. (38)

7. Conclusion

The main reason for poor outcome in patients with Wilms tumor was not receiving adequate chemotherapy after surgery. Dosesof chemotherapy received after surgerysignificantly affected treatment outcomes (p=0.026). Age at diagnosis, sex, duration of symptoms, stage at

diagnosis, and the protocol used did not predict survival.Further large studies are needed to establish the causes of treatment abandonment and to reduce its rate.

Limitation

The main limitations of this study were the small number of patients precluded proper statistical analysis and inference for many studied variables, and the fact that, because it was a retrospective medical record review, in which the data were collected during admission or follow-up, with no control of compliance to treatment or completeness of data collected, so some data were missing. Although surgical specimens were routinely sent for histological examination, results were not either collected from the pathology department, were not recorded or went missing. The retrospective design of this study didn't allow reliable staging. Despite the lack of accurate staging, it was assumed that, patients with tumor that were involving the surrounding structures during surgery are considered as a locally advanced tumor. So, the generalizability and reliability of results may be affected.

Recommendation

On the basis of the findings of the study, the recommendation is, completion of treatment regimens is needed.The reason for treatment refusal or abandonment should be documented on each respective medical folder so thattreatment abandonment will be addressed.Improvements in proper documentation, data collection, and tracing patients when they lost to follow are expected in a new study. There is need for public health measures to improve time to diagnosis, and improvement of facilities and healthcare funding to ensure compliance to all phases of standard therapy.

References

1.Ekenze SO, Agugua-Obianyo NE, Odetunde OA. The challenge of nephroblastoma in a developing country. Annals of oncology. 2006 Oct 1;17(10):1598-600

2. Breslow N, Olshan A, Beckwith JB, Green DM. Epidemiology of Wilms tumor. Medical and pediatric oncology. 1993;21(3):172-81.

3. Beckwith JB, Palmer NF. Histopathology and prognosis of Wilms tumor Results from the first national wilms' tumor study. Cancer. 1978 May;41(5):1937-48.4.L.M. Gommersall, M. Arya, I. Mushtaq, P. Duffy Current challenges in Wilms' tumor managementNat Clin Pract Oncol, 2 (2005), pp. 298-304

5.Pritchard-Jones K. Controversies and advances in the management of Wilms' tumour. Archives of disease in childhood. 2002 Sep 1;87(3):241-4.

6. Hadley LG, Rouma BS, Saad-Eldin Y. Challenge of pediatric oncology in Africa. InSeminars in pediatric surgery 2012 May 1 (Vol. 21, No. 2, pp. 136-141). WB Saunders.

7.Njuguna F, Martijn HA, Kuremu RT, Saula P, Kirtika P, Olbara G, Langat S, Martin S, Skiles J, Vik T, Kaspers GJ. Wilms tumor treatment outcomes: perspectives from a low-income setting. Journal of global oncology. 2017 Oct;3(5):555-62.

8.Rabeh W, Akel S, Eid T, Muwakkit S, Abboud M, El Solh H, Saab R. Wilms tumor: Successes and challenges in management outside of cooperative clinical trials. Hematology/oncology and stem cell therapy. 2016 Mar 1;9(1):20-5.

9.Wilde JC, Lameris W, Van Hasselt EH, Molyneux EM, Heij HA, Borgstein EG. Challenges and outcome of Wilms' tumour management in a resource-constrained setting. African Journal of Paediatric Surgery. 2010 Sep 1;7(3):159.

10.Dome JS, Perlman EJ, Graf N. Risk stratification for wilms tumor: current approach and future directions. American Society of Clinical Oncology Educational Book. 2014 May 13;34(1):215-23.

11.Dome JS, Graf N, Geller JI, Fernandez CV, Mullen EA, Spreafico F, Van den Heuvel-Eibrink M, Pritchard-Jones K. Advances in Wilms tumor treatment and biology: progress through international collaboration. Journal of Clinical Oncology. 2015 Sep 20;33(27):2999.

12. Bahoush-Mehdiabadi G, Habibi R, Shariftabrizi A, Vossough P. Epidemiologic survey of infantile cancer in Iran based on the data of the largest pediatric cancer referral center (Ali-Asghar Children Hospital), 1996-2005. Asian Pacific Journal of Cancer Prevention. 2014;15(3):1211-7.

13. Pleško I, Kramárová E, Stiller CA, Coebergh JW, Santaquilani M, EUROCARE Working Group. Survival of children with Wilms' tumour in Europe. European Journal of Cancer. 2001 Apr 1;37(6):736-43.

14. Park JR, Eggert A, Caron H. Neuroblastoma: biology, prognosis, and treatment. Hematology/oncology clinics of North America. 2010 Feb 1;24(1):65-86.

15. Nakata K, Colombet M, Stiller CA, Pritchard□Jones K, Steliarova□Foucher E, IICC□3 contributors. Incidence of childhood renal tumours: An international population□based study. International journal of cancer. 2020 Dec 15;147(12):3313-27.

16. Little J. Epidemiology of childhood cancer. IARC scientific publications. 1999 Aug..

17. Yang CP, Hung IJ, Jaing TH, Chang WH. Cancers in infancy: percent distribution and incidence rates. Acta PaediatricaTaiwanica= Taiwan er keyixue hui za zhi. 2006 Nov 1;47(6):273-7.

18. Green DM, Breslow NE, Beckwith JB, Ritchey ML, Shamberger RC, Haase GM, D'Angio GJ, Perlman E, Donaldson M, Grundy PE, Weetman R. Treatment with nephrectomy only for small, stage I/favorable histology Wilms' tumor: a report from the National Wilms' Tumor Study Group. Journal of clinical oncology. 2001 Sep 1;19(17):3719-24.

19. Cotton CA, Peterson S, Norkool PA, Takashima J, Grigoriev Y, Breslow NE. Early and late mortality after diagnosis of Wilms tumor. Journal of clinical oncology. 2009 Mar 10;27(8):1304.

20. Baez F, Bellani FF, Ocampo E, Conter V, Flores A, Gutierrez T, Malta A, Mendez G, Pacheco C, Palacios R, Sala A. Treatment of childhood Wilms' tumor without radiotherapy in Nicaragua. Annals of oncology. 2002 Jun 1;13(6):944-8.

21. Yildiz I, Yüksel L, Özkan A, Apak H, Celkan T, Danismend N, Büyükünal C, Söylet Y, Sarimurat N, Dervisoglu S, Aksoy F. Multidisciplinary approach to Wilms' tumor: 18 years of experience. Japanese journal of clinical oncology. 2000 Jan 1;30(1):17-20.

22. Al Fawaz IM, Ayas M, Rifai S, Khafaga Y, Al Shabanah M, Habib Z. Outcome of favorable histology Wilms' tumor: Experience at KFSH&RC, Saudi Arabia. Journal of clinical oncology. 2004 Jul 15;22(14_suppl):8557-.

23. Sidhom I, Hussien H, Kotb M, Anwer G, Aboul Naga S, Amin M, Ebied E, Ahmed H. Multidisciplinary Approach to Wilms' Tumor: 10 Years Experience of NCI, Egypt. Journal of Clinical Oncology. 2004 Jul 15;22(14_suppl):8544-.

24. Ekenze SO, Nwangwu EI, Ezomike UO, Orji EI, Okafor OO. Continuing barriers to care of Wilms tumor in a low□income country. Pediatric blood & cancer. 2019 Jan;66(1):e27416.

25. Yao AJ, Moreira C, Traoré F, Kaboret S, Pondy A, RakotomahefaNarison ML, Guedenon KM, Mallon B, Patte C. Treatment of Wilms Tumor in Sub-Saharan Africa: Results of the Second French African Pediatric Oncology Group Study. Journal of global oncology. 2019 Sep;5:1-8.

26Doghri R, Aloui A, Berrazaga Y, Boujelbene N, Driss M, Abess I, Fdhila F, Charfi L, Mezlini A, Mrad K. Analysis of prognostic factors of nephroblastoma in a Tunisian cohort. La TunisieMédicale. 2018 Mar 1;96(3):193-202.

27. Moreira C, Nachef MN, Ziamati S, Ladjaj Y, Barsaoui S, Mallon B, Tournade MF. Treatment of nephroblastoma in Africa: Results of the first French African pediatric oncology group (GFAOP) study. Pediatric blood & cancer. 2012 Jan;58(1):37-42.

28.Davidson A, Hartley P, Desai F, Daubenton J, Rode H, Millar A. Wilms tumour experience in a South African centre. Pediatric blood & cancer. 2006 Apr;46(4):465-71.

29. Madani A, Zafad S, Harif MH, Yaakoubi M, Zamiati S, Sahraoui S, Benjelloun A, Fehri M, Benchekroun S. Treatment of Wilms tumor according to SIOP 9 protocol in Casablanca, Morocco. Pediatric blood & cancer. 2006 Apr;46(4):472-5.

30. Abdallah FK, Macharia WM. Clinical presentation and treatment outcome in children with nephroblastoma in Kenya. East African medical journal. 2001;78(7):43-7.

31.Paintsil V, David H, Kambugu J, Renner L, Kouya F, Eden T, Hesseling P, Molyneux E, Israels T. The Collaborative Wilms Tumour Africa Project; baseline evaluation of Wilms tumour treatment and outcome in eight institutes in sub-Saharan Africa. European Journal of Cancer. 2015 Jan 1;51(1):84-91.

32. Israëls T, Molyneux EM, Caron HN, Jamali M, Banda K, Bras H, Kamiza S, Borgstein E, de Kraker J. Preoperative chemotherapy for patients with Wilms tumor in Malawi is feasible and efficacious. Pediatric blood & cancer. 2009 Oct;53(4):584-9.

33. Arora RS, Challinor JM, Howard SC, Israels T. Improving care for children with cancer in low□and middle□income countries—a SIOP PODC initiative. Pediatric blood & cancer. 2016 Mar;63(3):387-91.

34. Israëls T, Chirambo C, Caron HN, Molyneux EM. Nutritional status at admission of children with cancer in Malawi. Pediatric blood & cancer. 2008 Nov;51(5):626-8.

35. GRoss RE, NEUHAUSER EB. Treatment of mixed tumors of the kidney in childhood. Pediatrics. 1950 Dec;6(6):843-52.

36. Graf N, Tournade MF, de Kraker J. THE ROLE OF PREOPERATIVE CHEMOTHERAPY IN THE MANAGEMENT OF WILMS'TUMOR: The SIOP Studies. Urologic Clinics of North America. 2000 Aug 1;27(3):443-54.

37.Israëls T, Chirambo C, Caron H, de Kraker J, Molyneux E, Reis R. The guardians' perspective on paediatric cancer treatment in Malawi and factors affecting adherence. Pediatric blood & cancer. 2008 Nov;51(5):639-42.

38. Abuidris DO, Elimam ME, Nugud FM, Elgaili EM, Ahmed ME, Arora RS. Wilms tumour in Sudan. Pediatric blood & cancer. 2008 Jun;50(6):1135-7.

39. Harif M, Barsaoui S, Benchekroun S, Boccon-Gibod L, Bouhas R, Doumbe P, El Haffaf Z, Khattab M, Ladjadj Y, Mallon B, Moreira C. Treatment of childhood cancer in Africa. Preliminary results of the French-African paediatric oncology group. Archives de pediatrie: organeofficiel de la Societe francaise de pediatrie. 2005 Jun;12(6):851-3.

40. Wilde JC, Laméris VH, Molyneux EM, Hey HA, Borgstein ES. Retrospective study of patients with Wilms tumour in Malawi. InAbstract. Presented at Pan-African Paediatric Surgical Association meeting, Mombasa, Kenya 2006.

41Lemerle J, Voute PA, Tournade MF, Rodary C, Delemarre JF, Sarrazin D, Burgers JM, Sandstedt B, Mildenberger H, Carli M. Effectiveness of preoperative chemotherapy in Wilms' tumor: results of an International Society of Paediatric Oncology (SIOP) clinical trial. Journal of Clinical Oncology. 1983 Oct;1(10):604-9.

42. Godzinski J, Tournade MF, Dekraker J, Lemerle J, Voute PA, Weirich A, Ludwig R, Rapala M, Skotnicka G, Gauthier F, Moorman-Voestermans CG. Rarity of surgical complications after postchemotherapy nephrectomy for nephroblastoma. Experience of the International Society of Paediatric Oncology-Trial and Study. European journal of pediatric surgery. 1998 Apr;8(02):83-6.

43. Tournade MF, Com-Nougue C, De Kraker J, Ludwig R, Rey A, Burgers JM, Sandstedt B, Godzinski J, Carli M, Potter R, Zucker JM. Optimal duration of preoperative therapy in unilateral and nonmetastatic Wilms' tumor in children older than 6 months: results of the Ninth International Society of Pediatric Oncology Wilms' Tumor Trial and Study. Journal of clinical oncology. 2001 Jan 15;19(2):488-500.

44. Stefan DC, Stones DK. The South African Paediatric Tumour Registry-25 years of activity: forum-issues in child health. South African Medical Journal. 2012 Jul 1;102(7):605-6.51.S. C. Kaste, J. S. Dome, P. S. Babyn et al., "Wilms tumour: prognostic factors, staging, therapy and late effects," Pediatric Radiology, vol. 38, no. 1, pp. 2–17, 2008.

45. Israels T, Chagaluka G, Pidini D, Caron H, de Kraker J, Kamiza S, Borgstein E, Molyneux L. The efficacy and toxicity of SIOP preoperative chemotherapy in Malawian children with a Wilms tumour. Pediatric blood & cancer. 2012 Oct;59(4):636-41.

46.Poole J. The South African National Wilms Tumour Protocol. SIOP Africa. 2012;2102.

47. Dome JS, Fernandez CV, Mullen EA, Kalapurakal JA, Geller JI, Huff V, Gratias EJ, Dix DB, Ehrlich PF, Khanna G, Malogolowskin MH, Anderson JR, Perlman AN. Children's oncology group's 2013 blueprint for research: Renal tumors. Pediatr Blood Cancer 2013; 60: 994– 1000.

48. Israels T, Moreira C, Scanlan T, Molyneux L, Kampondeni S, Hesseling P, Heij H, Borgstein E, Vujanic G, Pritchard-Jones K, Hadley L. Clinical guidelines for the management of children with Wilms tumour in a low-income setting. Pediatr Blood Cancer 2013; 60: 5–11.

49. Israëls T, Kambugu J, Kouya F, El-Mallawany NK, Hesseling PB, Kaspers GJ, Eden T, Renner L, Molyneux EM. Clinical trials to improve childhood cancer care and survival in sub-Saharan Africa. Nature Reviews Clinical Oncology. 2013 Oct;10(10):599-604.

50. Libes J, Oruko O, Abdallah F, Githanga J, Ndung'u J, Musimbi J, Njuguna F, Patel K, White J, Axt JR, O'Neill Jr JA. Risk factors for abandonment of Wilms tumor therapy in Kenya. Pediatric blood & cancer. 2015 Feb;62(2):252-6.

51. Israels T, Borgstein E, Pidini D, Chagaluka G, de Kraker J, Kamiza S, Molyneux EM. Management of children with a Wilms tumor in Malawi, sub-Saharan Africa. Journal of pediatrichematology/oncology. 2012 Nov 1;34(8):606-10.

52.Ekenze SO, Agugua-Obianyo NE, Odetunde OA. The challenge of nephroblastoma in a developing country. Annals of oncology. 2006 Oct 1;17(10):1598-600.

53. Kutluk T, Varan A, Büyükpamukçu N, Atahan L, Çaglar M, Akyüz C, Büyükpamukçu M. Improved survival of children with wilms tumor. Journal of pediatric hematology/oncology. 2006 Jul 1;28(7):423-6

54.SSangkhathat S, Chotsampancharaen T, Kayasut K, Patrapinyokul S, Chiengkriwate P, Kitichet R, Maipang M. Outcomes of pediatric nephroblastoma in southern Thailand. Asian Pac J Cancer Prev. 2008 Dec;9(4):643-7.

55.Naguib SF, El Haddad AL, El Badawy SA, Zaghloul AS. Multidisciplinary approach to wilms' tumor: a retrospective analytical study of 53 patients. Journal of the Egyptian National Cancer Institute. 2008 Dec 1;20(4):410-23.

56. Yao W, Li K, Xiao X, Gao J, Dong K, Xiao X, Lv Z. Outcomes of Wilms' tumor in eastern China: 10 years of experience at a single center. Journal of Investigative Surgery. 2012 May 22;25(3):181-5.

57. Sultan I, Masarweh M, Ismael T, Al-Hussaini M, Almousa A, Ali HM, Rodriguez-Galindo C, Ghandour K. From upfront nephrectomy to preoperative chemotherapy and back: a single institution experience in the treatment of Wilms tumor. Journal of pediatrichematology/oncology. 2009 May 1;31(5):333-8.
58. Hung IJ, Chang WH, Yang CP, Jaing TH, Liang DC, Lin KH, Lin DT, Hsiao CC, Hsieh YL, Chen JS, Chang TT. Epidemiology, clinical features and treatment outcome of Wilms' tumor in Taiwan: a report from Taiwan Pediatric Oncology Group. Journal of the Formosan Medical Association. 2004 Feb 1;103(2):104-11.
59. Hadley, G. P. and Shaik, A. S. The Morbidity and Outcome of Surgery in Children with Pre-treated Wilms' Tumour: size matters. Pediatri. Surg. 2006; 22: 409-412.
60. Hadley, G. P. Can Surgeons fill the Void in the Management of Children with Solid Tumours in not-Developing Countries? Pediatri. Blood Cancer. 2010; 55: 16 – 17.
61. Kanavos, P. The Rising Burden of Cancer in the Developing World. Annals of Oncology. 2006; 17 (Supi 8): viii 15 – viii 14
62. Seyed–Ahadi, M. M., Khaleghnejad–Tabari, A., Mkshemirani, A., et al. Wilms' tumour, a 10-year retrospective study. Arch. Iran Med. 2007: 10: 65 – 69.
63. Yildiz, I., Yuksel, L., Ozkan, A., et al. Multidisciplinary approach to Wilms' tumour. 18 years' experience. JpnJ Clinical Oncol. 2000; 30: 17-20.
64. Asensio-Lahoz, L. A., Sandoval-Gonzalez, F., Abaitua-Bilbao, J., et al. Wilms' tumour in Cantabaria. Review of our cases (1979 – 1990). Arch. Esp. Urol. 1991; 44: 989 – 992.
65. Tenge CN, Were PA, Aluoch LH, Wekesa JW, Patel K, Kuremu RT. Management and outcome of patients with Wilms' tumour (nephroblastoma) at the Moi Teaching and referral hospital, Eldoret, Kenya. East African medical journal. 2012;89(4):121-7.
66. Yifru S, Muluye D. Childhood cancer in Gondar university hospital, Northwest Ethiopia. BMC research notes. 2015 Dec;8(1):1-5.
67. Tang F, Zhang H, Lu Z, Wang J, He C, He Z. Prognostic Factors and Nomograms to Predict Overall and Cancer-Specific Survival for Children with Wilms' Tumor. Disease markers. 2019 Dec 3;2019.
68. Bezuney AD, Groeneveld AE, Heyns CF. Pattern, clincal presentation and management of Wilms' Tumor in Moshi, Tanzania. African Journal of Urology. 2007 Aug 22;13(1):1-7.
69. Abdalla M, Hamid S. Improved outcome after Wilms tumor treatment in Sudan: a 10-year single-center experience. Authorea Preprints. 2020 Jul 30.
70. Hung IJ, Chang WH, Yang CP, Jaing TH, Liang DC, Lin KH, Lin DT, Hsiao CC, Hsieh YL, Chen JS, Chang TT. Epidemiology, clinical features and treatment outcome of Wilms' tumor in Taiwan: a report from Taiwan Pediatric Oncology Group. Journal of the Formosan Medical Association. 2004 Feb 1;103(2):104-11.
71. Mpirimbanyi C, Ndibanje AJ, Curci M, Kanyamuhunga A. Surgical Management and Outcomes of Wilms Tumor in Rwanda: A Retrospective Study of Patients Operated on at the University Teaching Hospital of Kigali-Rwanda. Rwanda Medical Journal.;78(2):29-34.

QUESTIONNAIR FOR THE ASSESSMENT PEDIATRIC WILMS' TUMOR TREATMENT OUTCOME AND FACTORS AFFECTING IT, IN JUMC PEDIATRIC ONCOLOGY WARD, A 5 YEAR RETROSPECTIVE STUDY

S. No	Question	Response Category	Skip ping
1 SOCIODEMOGRAPHIC DATA **MRN……**			
1.1	Age in months	……. months	
1.2	Sex	A. Male B. Female	
1.3	Residence	A. Urban B. Rural C. Unknown	
1.4	Care taker Occupation	A. Govt Employee B. Merchant C. Farmer D. Housewife E. Daily Laborer F. Others, Specify	
2. CLINICAL DATA			
2.1	Presenting Symptoms (2 or more options possible)	A. Abdominal swelling B. Abdominal Pain C. Hypertension D. Hematuria E. Others, Specify	
2.2	Duration of Illness (in days)	……...days	
2.3	Age at Diagnosis in months	…….. months	
2.4	Any Comorbidity/ concomitant illness identified at admission	A. Malnutrition B. Diabetes Mellitus C. Pneumonia D. Others, Specify E. No comorbidity identified	
2.5	Congenital anomaly/ syndromes identified	A. Aniridia B. Hemihypertrophy C. WAGR D. Denys-Drash Syndrome E. Beckwith Wiedemann syndrome F. Others, Specify G. No anomaly/syndrome identified	
3. PHYSISCAL FINDINGS AT DIAGNOSIS			
3.1	Anthropometry	A. Weight B. Height C. W/H D. H/A	

		E. W/A F. BMI G. MUAC	
3.2	Blood Pressure	A. Normal B. Hypertensive C. Hypotensive D. Not documented	
3.3	Abdominal Findings	A. No palpable mass B. Palpable mass not crossing the midline C. Palpable mass crossing the midline D. Others, Specify	
4. LABORATORY FINDINGS			
4.1.1	Hemoglobin (g/dl)	A. Normal B. Anemic C. Others, Specify D. Not Documented	
4.1.2	Platelet Count (x1000)	A. Normal B. Thrombocytopenia C. Thrombocytosis D. Not Documented	
4.2	Renal Function Test	A. Normal B. Abnormal C. Not Documented	
4.3.1	Proteinuria	A. Positive B. Negative C. Not Documented	
4.3.2	Hematuria	A. Positive B. Negative C. Not Documented	
5. HOW IS THE DIAGNOSIS MADE			
5.1	How was the diagnosis made?	A. Imaging B. Open Surgical Biopsy C. Image Guided Biopsy D. Others, Specify	
5.2	Imaging modality used for the diagnosis (more than one option possible)	A. Ultrasound B. Intravenous Urography C. CT scan D. MRI	
5.3.1	maximum diameter of the tumor in cm before chemotherapy		
5.3.2	maximum diameter of the tumor in cm after chemotherapy		
5.4	Any evidence of venous tumor thrombus	A. Ipsilateral renal vein B. Up to the hepatic vein C. Below the diaphragm D. Above the diaphragm E. No venous tumor thrombus	

5.5	Tumor Laterality	A. Right B. Left C. Solitary Kidney D. Bilateral	
5.6	Any evidence of Nephrogenic Rest or Suspicious lesion in the kidney	A. Ipsilateral kidney B. Contralateral kidney C. Bilateral kidney D. No evidence	
5.7	Evidence of Metastases	A. Liver B. Lung C. Both Liver and Lungs D. No evidence of metastatic disease	
5.8	How was lung metastasis diagnosed?	A. Clinical Suspicion B. Chest X-ray C. Chest CT scan D. Others, Specify	
6. STAGE OF THE DISEASE			
6.1	Stage at Diagnosis	A. Localized B. Locally Advanced C. Distant Disease	
7. HISTOPATHOLOGY FINDINGS			
7.1	Histology report available	A. Wilms tumor with favorable histology B. Wilms tumor with focal anaplasia C. Wilms tumor with diffuse anaplasia D. Others, Specify E. Not done (Reason)	
7.2	Lymph Node status	A. Positive B. Negative C. Not Assessed/Reported	
8. TREATMENTS PROVIDED			
8.1 Date of Diagnosis……..……. (DD/MM/YYYY) 8.2 Date of initiation of treatment……. (DD/MM/YYYY)			
8.3	Treatment Protocol used	A. SIOP B. NWTSG	

		C. INCTR D. D. Others, Specify	
8.4	Chemotherapy regimen given (Number of doses and at which week)	A. VCR+ActD B. VCR+ActD+Dox C. VCR+ActD+Dox+Cyclo D. VCR+ActD+Dox+Cyclo+Etop	
8.5	Date of Surgery done	……. (DD/MM/YYYY)	
8.6	Type of Surgery Done	A. Radical Nephrectomy with Lymphadenectomy B. Radical Nephrectomy without Lymphadenectomy C. Debulking Surgery D. Incisional Biopsy alone E. Not done	
8.7	Tumor rupture during Surgery	A. Yes B. No	
8.8	Number of doses of chemotherapy received before surgery		
8.9	Radiotherapy Given	A. Flank alone B. Hemiabdomen C. Entire abdomen D. Chest E. Not given	
9. TREATMENT OUTCOMES			
9.1 Date of completion of treatment……..……... (DD/MM/YYYY) 9.2 Last Date of follow up……..…. (DD/MM/YYYY)			
9.3	Was the treatment completed according to the protocol	A. Yes B. No	
9.4	Documented Response while on treatment	A. Complete remission B. Partial remission C. No change seen D. Progressive disease while on treatment	
9.5	Documented outcome at the last follow up	A. Cured B. Relapsed C. Abandoned the treatment D. Lost from follow up E. Died/Presumed to die	
9.6	Possible cause of Death	A. Tumor Related B. Treatment Related C. Unknown D. Others, Specify	