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Wilm's tumor: Presentation and outcome at Kilimanjaro Christian Medical Center

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Abstract

Objective: The purpose of the present study was to identify the gaps in the management of Wilms' tumor which resulted in an inferior outcome and to see if there is any improvement since the last study and to come up with recommendations to improve the outcome of Wilms' tumor. **Patients and Methods:** This was a retrospective hospital based study at Urology Institute of Kilimanjaro Christian Medical Centre. Patients operated for Wilms' tumor between January 2006 and December 2013 were identified and the medical records of the 46 patients eligible for the study retrieved. The relevant information was entered into the prepared data collection format. The data was cleaned, summarized and analysed using SPSS version 17. **Results:** Patients with Wilms' tumor presented late to KCMC. There was no undue delay in reaching at diagnosis. From the 46 total number of patients in this study 20 (43.5%) of patients received neoadjuvant chemotherapy while 26 (56.5%) had an upfront nephrectomy. The one year recurrence free survival was 32.6% with a high rate of lost to follow up (41.3%), perioperative mortality of (10.8%), and recurrence rate of (26.8%). **Conclusion:** There was no improvement in the outcome of WT at KCMC compared to the last report 8 years back. Patients still present late to health institutions, there is high rate of lost to follow up and the prognosis of Wilm's tumor in this part of Africa is still dismal.

Keywords: Wilm'stumor, Presentation, Outcome.

INTRODUCTION

Wilms' tumor is the second most common childhood cancer in Africa and while survival from Wilms' tumor exceeds 90% at 5 years in developed nations accounting for 6% to 7% of all childhood cancers [1]. In children less than 15 years of age, the annual prevalence rate is about 7 to 10 cases per million [2-3]. Black – African children have an increased prevalence of WT (11 cases per million children <15 years of age) compared with whites (8 cases per million) [4]. Some studies have mentioned some hypothetical risk factors for Wilms' tumour such as occupational, environmental, and life style factors. Although some studies have suggested that a number of parental exposures might be associated with an increased risk of Wilms' tumor, very few have been found conclusively associated [1].

Children with Wilms' tumour most of them are asymptomatic until when they present with a palpable smooth abdominal mass picked incidentally in 90% of children. Some children may present with Abdominal pain, gross haematuria, and fever at diagnosis [1,6]. Children from developing nations almost always present with abdominal mass though additional features might be there. And compared to developed nations patients with WT from developing countries present late [7-10].

Ultrasonography is the first study performed in most children with an abdominal mass. Doppler ultrasonography is particularly helpful in excluding intracaval tumor extension that occurs in 4% of WT patients. The most important determinants of outcome in children with WT are the histopathology and tumor stage [1].

PATIENTS AND METHODS

This is a retrospective hospital based study conducted at Kilimanjaro Christian Medical Centre, Moshi, Tanzania. KCMC is a tertiary referral hospital for central and northern zones of Tanzania.

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The patients operated for Wilm'stumor between January 2006 and December 2013 were identified from the hospital operation Theatre registry. A total of 55 patients were identified. From these 1 patient had a histologic diagnosis of Renal Cell Carcinoma.In 4 patients the histology result could not be found and in 4 patients the hospital records could not be traced. So 9 patients were excluded. The medical records of the remaining 46 patients were retrieved. The information needed for the study entered into a format prepared for this purpose. The data was analysed using SPSS version 17. Ethical clearance was approved by the Kilimanjaro Christian Medical University College Research and Publications Committee (No 682). All patients' information was kept confidential.

RESULTS

The mean age of patients at presentation was 53 months; the median age was 48 months with the range of 7 to156 months. The male to female ratio was 1.3: 1.Forty two (91.3%) of patients presented with the chief complaint of abdominal swelling another two (4.4%) patients presented with the main complaint of abdominal pain and 2 (4.4%) patients presented with the main complaint of hematuria. Twenty seven patients had additional complaint besides the chief complaint. Patients presented to KCMC after a mean of 2.4 months with a range of one week and one year.

All patients had abdominal mass on examination. 16 (34.8%) patients had additional physical findings.

Ultrasound and IVU were done for the majority of the patients and the two modalities combined were accurate in 42 of the 46 patients in whom treatment was initiated based only on the imaging results. This has resulted in no patient receiving chemotherapy for a benign pathology. The other 4 patients were diagnosed by FNAC, which was accurate in all the 4 patients. Staging was done based on clinical findings and imaging results. The biopsy results were not helpful to differentiate between stage one and stage two. So stage one and two are lumped together. The stage of WT at presentation was; Stage I and II-16 (34.8%), Stage III – 27 (58.7%), Stage IV- 3 (6.5%)

Establishing the diagnosis of WT took a mean of 2.52 days after patients presented to KCMC with the range of 1 and 21 days. Treatment was initiated on the average in 16 days after patients presented to KCMC with a range of 4 to 83 days.

Twenty (43.5%) patients received neoadjuvant chemotherapy. But the number of cycles patients received was not standardized and it depended on the clinical judgment of the managing urologists of the response of the tumor to the chemotherapy based on the abdominal girth and size reduction on palpation. Most patients received between 1 and 3 cycles before surgery.

The tumor was resectable in all but one patient in whom biopsy only was taken.

In 7 (15.2%) patients there was intraoperative tumor spillage. From the seven intraoperative tumor spillage 6 (85.7%) occurred in patients who did not receive adjuvant chemotherapy. Intraoperative blood transfusion was required in 20 (43.5%) of patients. When it comes to perioperative mortality, 5 (10.9%) patients died in hospital during the first three post-operative days 4 of whom died within hours of the surgery. 41 (89.1%) patients were discharged home and all were started on adjuvant chemotherapy before discharge.

From the 41 patients 16 (39%) completed their chemotherapy course. Two (4.9%) were transferred to other hospital to complete their chemotherapy. From the 23 patients who didn't complete their adjuvant chemotherapy 19 (82.6%) were lost to follow up and 4 (17.4%) died in hospital during their follow up.All in all recurrence was detected in 11 (26.8%) of the 41 patients during the follow up and the site of recurrence was local in 5 patients, in the chest in 3 patients and other sites in 3 patients. The recurrence was noted after a mean of 7.3 months of the surgery with a range of 3 to 12 months.

From the 46 patients included in this study in 30 patients the pathologists sub classified the type of WT. 27 patients had a favourable histology, 1 patient had anaplastic WT and 2 patients had blastemal predominant WT. In 16 (34.8%) patients no histologic sub classification was given.

The one year overall survival was 39.1%, the one year recurrence free survival was 32.6%, 10.8% died during the immediate post-operative period and 8.7% died in hospital during their follow up. From the patients who died in hospital during the follow up 3 died from recurrence and one died from blood transfusion reaction; 41.3% of patients were lost to follow up.

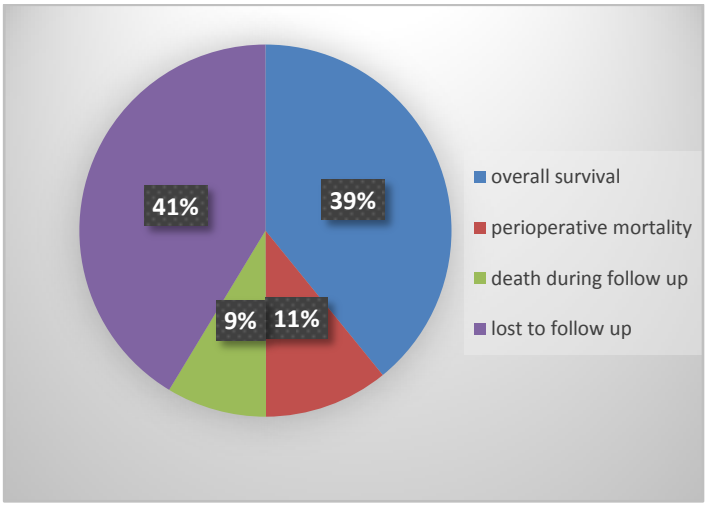

Figure 1: Chart showing the overall outcome of Wilm'sTumor Management at KCMC

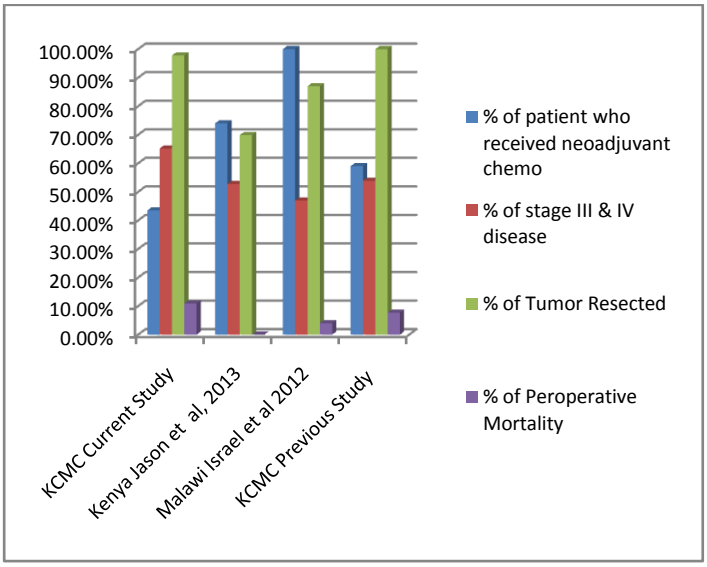

Figure 2: Chart comparing percentage of Neoadjuvant Chemo, Stage of the Disease, Percentage of Tumor Resected and Perioperative Mortality

DISCUSSION

The mean age at presentation is higher than reports in the literature (53 months versus 41-45 months) [4, 7]. The male to female ratio of 1.3:1 is similar to other reports from Africa [4,11] but different from the large studies of the NWTSG which is almost 1:1. These differences can be explained by the difference in the number of patients studied. The

presenting complaint of abdominal swelling found in 42 (91.3%) of patients is comparable to other studies where the majority of patients presented with abdominal swelling [8, 12].

Ultrasound and IVU were done for the majority of the patients and the two modalities combined were accurate in 42 of the 46 patients in whom treatment was initiated based only on the imaging results. This has resulted in no patient receiving chemotherapy for a benign pathology. It also affirms that neoadjuvant chemotherapy can be given without histologic diagnosis in the majority of cases.

Establishing the diagnosis took only an average of 2.5 days and initiating treatment took only 16 days compared to 15.5 days and 41.2 days respectively in another African study [4].

This might reflect the level of expertise at the centre. Unfortunately these gains in reaching diagnosis and initiating treatment did not translate in better overall survival probably due to many reasons notable among which are the late presentation of patients to the centre and the high LTFU rate. Twenty (43.5%) patients received neoadjuvant chemotherapy. This is less than the number of patients who received neoadjuvant chemotherapy in the same centre8 years back which was 59% [11]. This result is understandable taking into consideration the policy of the centre to give neoadjuvant chemo on individual bases. The tumor was resectable in all but one patient. This is higher than what was achieved in Kenya (69.9%) and Malawi (87%) [4, 9] but similar to the previous study from the same centre.

The table shows with less patients given preoperative chemotherapy and with more patients with advanced stage disease all tumors but one were resected over a two decade period at KCMC. This might indicate the surgeons were over courageous during the surgeries and might also explain the high perioperative mortality seen in the centre.

In 7 (15.2%) patients there was intraoperative tumor spillage. This is high compared to two studies from India [12-13] where the patient characteristics are similar but neoadjuvant chemotherapy was given to all patients. These two studies reported no intraoperative tumor spillage. This result corroborates the finding that neoadjuvant chemotherapy decreases the risk of intraoperative tumor spill as has been shown in SIOP trials.

In this study also 6 of the 7 tumor spillages occurred in patients who did not receive preoperative chemotherapy. This finding becomes more important when one considers the policy of the centre to give neoadjuvant chemotherapy to relatively large tumors which are judged unresectable. So it is in the relatively small tumors which did not get pre-operative chemotherapy that the spillages were occurring. Of note no recurrence was noted in our patients with intraoperative tumor spill during their follow up.

The perioperative mortality of 10.9% is high compared to a report from neighbouring Malawi where there was 4% perioperative mortality [9]. As can be seen from table 7 with less percentage of patients on neoadjuvant chemotherapy and with more patients with stage III- IV disease, more of the tumors were resected at KCMC. This might suggest again the surgeons might have been aggressive during the nephrectomy and that might have contributed to the increased perioperative mortality. The other possible factor is not giving neoadjuvant chemotherapy to all patients.

Forty one patients were started on adjuvant chemotherapy but only 18 (43.4%) of them completed their chemotherapy course. 19 (41.3%) of the total population of the study were lost to follow-up. The proportion of LTFU is comparable to the 50 % from a Kenyan study but much higher than the 10.3% reported from the same centre 8 years back [4, 11]. Why there is such dramatic increase in the number of LTFU is difficult to answer from this study as this is out of the scope of the study. However this is one of the big gaps identified in this study and needs to be addressed by future prospective studies.

The one year recurrence free survival (32.6%) is comparable to reports from other African studies. A study from Malawi reported 46% survival with a median follow-up of 16 months (range from 1 to 52 months) [9] and a Kenyan study showed a two year disease free survival of 34.7 % [14]. The previous study from KCMC reported a one year recurrence free survival of 35.9 % [11].

CONCLUSION

As in most studies from Africa, this study has found patients with WT present late to medical centres so the disease is caught at an advanced stage which makes management of the disease difficult and the outcome grim from the start. The mortality and morbidity from the disease is not acceptable. There is high rate of lost to follow up. Measures should be in place to raise awareness about the disease to catch it early, to decrease the rate of lost to follow up. Neoadjuvant chemotherapy should be given for all patients in developing countries. And the health systems of Africa should give the due emphasis to paediatric oncology.

Conflict of interests

The authors declare no conflict of interests.

Authors' contributions

WEW*:* designed the study, collected data, performed data analysis and wrote the report with a manuscript**.** OVN, BF; participated in the study design and manuscript preparation.

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