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# Epidemiology, Clinical Features and Management of Wilms Tumour at the Mother and Child Center-CBF, Yaounde

## *Aspects épidémiologiques, cliniques et thérapeutiques de la tumeur de Wilms au Centre Mère et Enfant-FCB, Yaoundé*

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**Keywords:** Childhood, Cameroon, Mother and Child Center,

**ABSTRACT**

**Introduction.** Nephroblastoma or Wilms tumour is the most common kidney tumour in children. It is a curable tumour with a well-codified treatment. However, few data are available in Africa and Cameroon on this pathology. This article describes the epidemiological, clinical and therapeutic profile of Wilms tumours in children monitored at the Mother and Child Center of the Chantal Biya Foundation (MCC-CBF) in Yaounde. **Patients and methods.** We conducted a cross sectional retrospective descriptive study. Data were collected from patients aged 0 to 15 years from January 2008 to December 2018 (a period of 11 years). The analysis was done using the software Epi Info 7.2.2.16. **Results** We had 158 cases. Mean age was 4.54 ± 3.27 (range, 0.2 to 14 years), and a male predominance (sex ratio of 1.1: 1). The most common clinical sign was abdominal distension (35.29%). Forty one children (37.27%) had disseminated disease mainly in the lungs (42.11%) and liver (31.58%). One hundred and eight patients (77.14%) received complete treatment; 101 (63.92 %) had remissions and 45 (28.48 %) died. The overall survival at 5 years was 70 %. **Conclusion** In our context, Wilms tumour is a disease of the young child under 7 years old. Most children come late with advanced disease. Some cases still do not receive treatment.

**RÉSUMÉ**

**Introduction** le néphroblastome ou tumeur de Wilms est la tumeur rénale la plus courante chez les enfants. C'est une tumeur guérissable avec un traitement bien codifié. Cependant, peu de données sont disponibles en Afrique et au Cameroun sur cette pathologie. Cet article décrit le profil épidémiologique, clinique et thérapeutique des tumeurs du Wilms chez les enfants suivis au Centre Mère-Enfant de la Fondation Chantal Biya (CME-FCB) à Yaoundé. **Patients et méthodes** nous avons mené une étude descriptive rétrospective. Les données ont été recueillies auprès de patients âgés de 0 à 15 ans entre janvier 2008 et décembre 2018 (une période de 11 ans). L'analyse a été effectuée à l'aide du logiciel Epi info 7.2.2.2.16. **Résultats** nous avons colligé 158 cas. L'âge moyen était de 4,54 ± 3,27 ans (intervalle de 0,2 à 14 ans), avec une légère prédominance masculine (sex-ratio égal à 1,1/1. Le signe clinique le plus fréquent était la distension abdominale (35,29 %). Quarante un enfants (37,27 %) avaient une maladie disséminée principalement dans les poumons (42,11 %) et le foie (31,58 %). 108 enfants (77,14 %) ont reçu un traitement complet. Parmi eux, 101(63,93%) ont bénéficié d'une rémission, tandis que 45 (28,48 %) sont décédés. La survie globale à 5 ans était de 70 %. **Conclusion** dans notre contexte, la tumeur de Wilms est une maladie du jeune enfant de moins de 7 ans. La plupart des patients arrivent en retard avec une maladie avancée. Certains cas ne reçoivent toujours pas de traitement.

## INTRODUCTION

Malignant disease is becoming a major health concern in almost equal proportions to communicable diseases and malnutrition in developing countries [1]. The World Health Organization (WHO) in 2008 estimated 500 000 deaths from cancer in Sub-Saharan Africa [2]. Of the 175 000 children who develop cancer annually, more than 150 000 live in low- and middle-income-countries (LMICs). Childhood cancer remains the leading cause of disease-related mortality in children [3]. In Cameroon, about 15 000 new cases are diagnosed annually [4] throughout the country as compared to 10 000 cases a decade ago [5] , and childhood cancer constitutes about 10 % of all malignancy [6,7]

Wilms' tumour (Nephroblastoma), the most common genitourinary malignancy of childhood [8], is an embryonal tumour of renal origin [9] and ranks fifth in incidence among the solid tumours of childhood. The treatment of Nephroblastoma (NPH) has been improved in the past two decades, with the aid of multimodal therapy protocols [10].

Edwards et al in their descriptive qualitative study of childhood cancer challenges in South Africa found a

significant lack of public information about cancer, lack of knowledge and low awareness of early signs of cancer of cancer by primary care staff [11]. Due to the scarcity of data in our context, we decided to carry out this study to raise local data on the prevalence, clinical profile and treatment options of the disease, so as to ameliorate standard of care. Data regarding cancer incidence are important for several reasons. Cancer is an endemic disease with considerable variation in frequency according to the site incidence. It is imperative to give attention to children with cancer, who have an increasing likelihood of cure with appropriate treatment. Also amongst other findings, Onuigbo et al discovered peak age of incidence of NPH to be 24-59 months contrary to the French authors' 1-5yrs [12]. It is therefore important to study and compare these data with those in our setting as a misconception of this leads to adverse outcomes and poor prognosis. This led us to carry out this study entitled: Epidemiological, Clinical and Therapeutic Profiles of Retroperitoneal Tumours in the Paediatric Population at the Mother and Child Center of the Chantal Biya Foundation (MCC-CBF), Yaoundé to show that there are profiles particular to our setting.

## PATIENTS AND METHODS

The research proposal was reviewed and approved by the institutional Ethical Review Board of the Faculty of Medicine and Biomedical Sciences (IERB-FMBS) and by the administration of the MCC-CBF. This was a descriptive, retrospective study carried out in the Haematology and Oncology unit at the MCC-CBF; one of Cameroon's largest children hospitals, housing one of the two structures in the country specialized in the treatment of childhood cancer and receives children with paediatric malignancies from all over the national territory. The study was carried out over a 7 months period from November 2018 to May 2019. The collection of information for the study was done under strict respect of patient confidentiality. Information collected was used for the sole purpose of the study. Also, all patient files were examined within the archive of this institution without any tempering or modification of their contents.

### Patients

Thorough analysis of the registers of the said unit was done, and a list was established of patients diagnosed of or hospitalised for NPH confirmed by the chief of service from January 1, 2008 to December 31, 2018. Using this list, medical records were searched for and obtained at the archives of the unit. All children less than 15 years old with histological or radiological diagnoses of NPH. We excluded all cases whose files were inexplorable.

### Data collection and analysis

Data from validated questionnaires was entered into Microsoft excel 2013 spread sheets. Visual checking for obvious errors and inconsistencies in the data was done. All data were imported into the statistical software Epi Info version 7.2.2.16 for analysis. The categorical variables were expressed in frequency and percentage, and the numerical variables were expressed using averages, standard deviations, minimums, medians, maximums and valid observation totals. To compare gender versus stage, and age versus stage, the likelihood ratio test was used. Associations between variables in the study were analysed using Fisher's exact or Chi-square test. Survival curves were generated using Kaplan-Meier's estimator method. The results were presented in figures and tables, generated by Microsoft Excel 2013.

## RESULTS

All cases were gotten at the haematology and oncology unit of the MCC-CBF.

### Patient inclusion

Our study was carried out from the cases in the registers and medical records starting from January 2008 to December 2018. During this 11-year period, there were 159 cases of Wilms tumour identified. Of these 159, 1 (0.63 %) case was excluded for age strictly greater than 15 years. Overall, 158 cases were included in this study, and the data from them were analysed.

### Quality of data

Our data were retrieved from patient files and completed with information from the registers.

### Age and sex

There were 74 (47 %) cases were female while 84 (53 %) were male giving a sex ratio of (M/F=1.1:1). Ages ranged from 0.2 to 14 years with a mean age of 4.54 ± 3.27 years and the most common age was 1 year. The peak age was 4 to 7 years with 55 (34.81 %) cases for NPH followed by 2 to 4 years with 42 (26.58 %) cases (Figure 1).

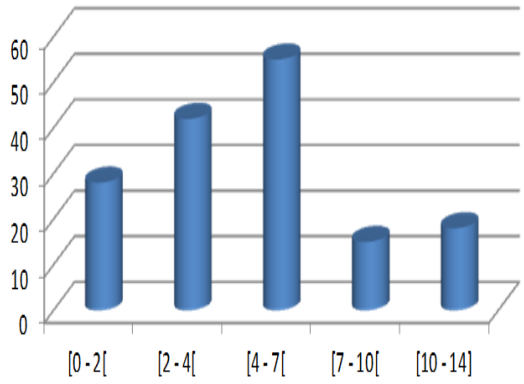


**Figure 1**: Age group of patients

There was an increase trend seen in the hospital incidence of both NPH cases from 2008 to 2018. The year 2018 recorded the highest number of cases in our study 18 (11.4 %) while 2009 registered the least number of cases 8 (5.1 %) (Table I).

**Table I: Incidence per year of NPH at the CBF**

| *Year* | *2008* | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| *n* | *16* | 8 | 14 | 17 | 16 | 14 | 17 | 12 | 12 | 14 | 18 | 158 |
| % | 10.1 | 5.1 | 8.9 | 10.8 | 10.1 | 8.9 | 10.8 | 7.6 | 7.6 | 8.9 | 11.4 | 100.0 |

Most of the cases of retroperitoneal tumours occurred before the age of 7, 125 (79.11 %) cases.

**Clinicopathological Features**

Out of the 158 cases, data on revealing clinical sign was gotten in 119 (75.32 %) cases. Overall, abdominal distension was the most common sign that led to the suspicion of NPH, 42 (35.29 %) cases. The least in our case was other masses; 1 (0.84 %) cases.

Amongst the cases with data available, 69 (62.73 %) were localized while 41 (37.27 %) were metastatic. The age groups with the highest number of metastasis were 4 to 7 years with 19 (46.34 %) cases (Table II).

**Table II: Stage at Presentation by Sex and Age Group**

| Age Group (years) | **Stage at Presentation** | | | | | |
|---|---|---|---|---|---|---|
| | Localized | | | Metastatic | | |
| | *Overall* | M | F | *Overall* | M | F |
| | *n* | n | n | N | n | n |
| 0 - < 2 | 15 | 7 | 8 | 3 | 1 | 2 |
| 2 - < 4 | 22 | 10 | 12 | 10 | 8 | 2 |
| 4 - < 7 | 24 | 9 | 15 | 19 | 9 | 10 |
| 7 - < 10 | 2 | 0 | 2 | 6 | 4 | 2 |
| 10 – 14 | 6 | 4 | 2 | 3 | 3 | 0 |
| Total | 69 | 30 | 39 | 41 | 25 | 16 |

The most common predispositions were exposure to chemical substances, genitourinary malformations and other malformations at 6 (3.80 %) cases each. There was 1 (0.63 %) case of Denys-Drash syndrom.

Diagnosis was based mainly on clinical and imaging. Of our 158 cases of NPH, data on clinical signs at entry was available in 115 (72.78 %) cases. The most common sign was palpable mass in the abdomen 100 (65.36 %).

Of the 158 cases in our study, we got the lag time from onset of first symptom to time of consultation for 152 (66.09 %) cases. The range was from 0 to 156 weeks, with a mean time lag of 13.79 ± 23.87 weeks. 75 % of our cases came for consultation at 19 weeks or lesser. The median time was 8 weeks, while the most frequent time was 4 weeks. When lag time was compared with disease stage we found that longer lag time was associated with advanced stages of disease (Table III).

**Table III: Comparison between staging and time from onset of signs and symptoms (weeks) for NPH using the non-parametric Kruskal Wallis test. (p= 0.0697)**

| Lag time (weeks) | **Stage 1** | **Stage 2** | **Stage 3** | **Stage 4** | **Stage 5** |
|---|---|---|---|---|---|
| Average±standard deviation | 8.4 ± 8.2 | 5.6 ± 6.1 | 7.6 ± 7.1 | 20.1±30.2 | 17.5 ± 28.3 |
| Median (minimum-maximum) | 5 (0-36) | 4 (1-20) | 6 (0-24) | 15 (0-156) | 4 (2-60) |
| Total | 37 | 9 | 17 | 36 | 4 |

Data on the site of the tumour was gotten for 99 (62.66 %) cases. 93 (93.94 %) cases were unilateral and only 6 (6.06 %) cases where bilateral. 52 (52.53 %) were located on the right side. 8 % of females and 4.08 % of males had bilateral tumours.

Among 41 cases of metastasis, there were 57 metastasis sites. The most frequent location was the lungs (42.11 %) of all metastasis sites, followed by the liver with 18 (31.58 %) cases. The location of metastases when compared for male and female was nearly the same except for the liver metastasis in which the males had a significantly higher number than the females.

Data on the histological type was available for 67 (42.41 %) out of the 158 cases. The most common type was the intermediate risk at 34 (51 %) cases of which the most frequent subtype was Triphasic at 20 (29.85 %) cases. This was followed by the high risk group at 19 (28.3 %) cases consisting only of Blastemal subtypes (Table IV).

**Table IV: Risk groups with Histological types by sex**

| Risk Group Histological Type | Overall | | Male | | Female | |
|---|---|---|---|---|---|---|
| | *n* | %* | N | %[a] | n | %[b] |
| **Low Risk** | 11 | 16.42 | 6 | 17.14 | 5 | 15.63 |
| Mesoblastic | 2 | 2.99 | 1 | 2.86 | 1 | 3.13 |
| Cystic | 9 | 13.43 | 5 | 14.29 | 4 | 12.50 |
| Completely Necrotic | 0 | 0.00 | 0 | 0.00 | 0 | 0.00 |
| **Intermediate Risk** | 34 | 50.75 | 15 | 42.86 | 19 | 59.38 |
| Epithelial | 3 | 4.48 | 1 | 2.86 | 2 | 6.25 |
| Stromal | 7 | 10.45 | 2 | 5.71 | 5 | 15.63 |
| Triphasic | 20 | 29.85 | 10 | 28.57 | 10 | 31.25 |
| Regressive | 4 | 5.97 | 2 | 5.71 | 2 | 6.25 |
| Focal Anaplasic | 0 | 0.00 | 0 | 0.00 | 0 | 0.00 |
| **High Risk** | 19 | 28.36 | 11 | 31.43 | 8 | 25.00 |
| Blastemal | 19 | 28.36 | 11 | 31.43 | 8 | 25.00 |
| Diffuse Anaplasic | 0 | 0.00 | 0 | 0.00 | 0 | 0.00 |
| Others | 3 | 4.48 | 3 | 8.57 | 0 | 0.00 |
| **Total** | 67 | 100.00 | 35 | 100.00 | 32 | 100.00 |

**Therapeutic Profile**

Of the 158 cases recorded in our study, we found data on treatment in 140 (88.61 %) cases. 132 (94.29 %) underwent some form of treatment while 8 (5.71 %) did not receive any treatment regimen for malignancy. 24 (17.14 %) cases were treated with chemotherapy only, while 108 (77.14 %) with combined chemotherapy and surgery.

Both low and intermediate risk cases received treatment according to the GFAOP 2005; ACT D/VCR/ADRIA (Actinomycin D, Vincristine, and Doxorubicin) protocol. For the high risk cases chemotherapy consisted of VP 16/CARBO/CYCLO/ADR (Etoposide, Carboplatin, Cyclophosphamide, Doxorubicin). Surgery in all cases consisted of radical or partial nephrectomy. The duration of treatment was greatly variable, 47 (37.01 %) received treatment for at least 3 months while 12 (9.45 %) at least for 6 months and 68 (53.54 %) for more than 6 months. The mean and median duration of treatment was 5.37 ± 3.85 and 6 months (range 0 - 16).

**Outcome**

20 (12.26 %) cases abandoned the treatment mainly due to refusal of diagnosis, 17 (10.76 %) cases witnessed a relapse, 101 (63.92 %) had remissions and 45 (28.48 %) patients died. The outcome of 12 (7.59 %) cases was otherwise not specified.

Deaths due to retroperitoneal tumours accounted for 9 % in 2016 to 24 % in 2010 of all deaths registered at the MCC-CBF. The total deaths due to retroperitoneal tumours alone account for 14.90 % of all deaths at the CBF within the study period (Figure 2).

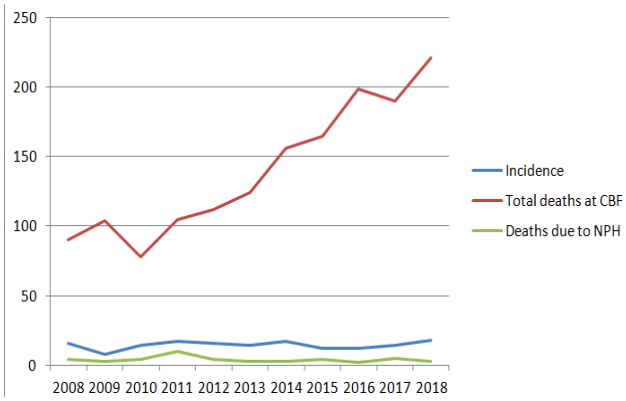


**Figure 2:** Incidence and deaths due to NPH

The Kaplan-Meier survival probability curve was plotted for a period of 11 years. The overall survival of NPH at 2 years and 5 years was 72 % and 70 % respectively (Figure 3).

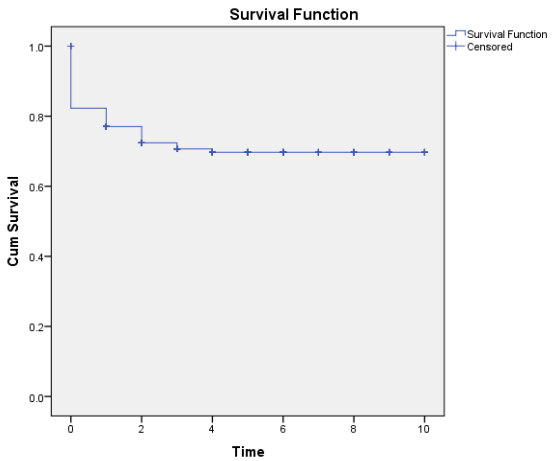


**Figure 3**: Overall survival rates of NPH

The 5-year overall survival rate of those who received complete treatment (complete chemotherapy and surgery) was 92 % whereas for those who did not complete treatment, it was at 21 % (Figure 4).

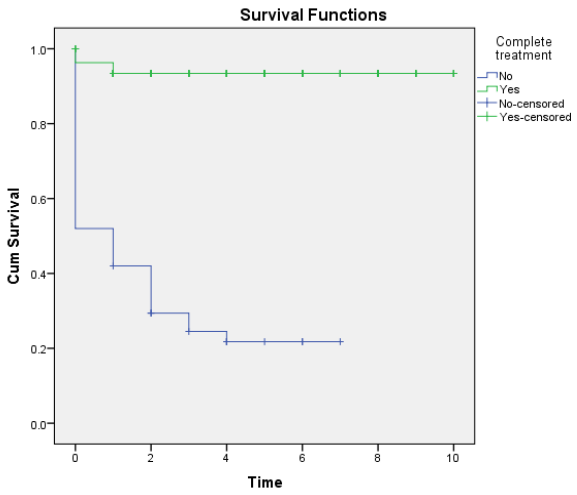


**Figure 4**: Overall survival of complete and incomplete treatment (p= 0.000)

## DISCUSSION

We sought to describe the epidemiological, clinical and therapeutic profiles of retroperitoneal tumours in children, a retrospective study from January 2008 to December 2018 of patient medical records with clinical, and paraclinical diagnosis of retroperitoneal tumours at MCC-CBF. We included only children, aged 15 years and below, recording an overall of 158 cases during this 11-year period. The male/female sex ratio was 1.1:1 Most of cases occurred before the age 7 years. Abdominal distension was the most common presenting sign. Many patients presented late with advanced disease with a mean time lag of 15.91 ± 23.87 weeks. Overall 5 year survival was at 70 %.

We had a male to female ratio of 1.1:1. Male predominance was reported by Rais *et al* in Morocco [13,14]. Some of the possible explanations for this might be that, the male gender integration into society is early and are more frequently exposed to risk factors like pesticides, chemical solvents, infections that predispose to development of malignancies than females.

The peak age was 4 to 7 years with 55 (34.81 %) cases for NPH followed by 2 to 4 years with 42 (26.58 %) cases. This is similar to the findings of other African authors [12,15]. Our findings however differ with that of Illade *et al* in Spain who had a much lesser peak age. This phenomenon could be explained by the fact that in developed countries there are more screening programs and better awareness of the disease.

The median time to medical visit was 8 weeks (0 - 156) and 75 % of our cases had come by 19 weeks. This is significantly higher than the findings of Rais *et al* and, who found median time of 4 weeks with 84 % of children consulting by 12 weeks [14]. There was also a higher occurrence of advanced stage of disease in patients with longer lag time. This might be explained by the fact that childhood treatment centres are highly centralized in Cameroon, being available just in 2 regions of the country. Also, the unavailability of screening programs could be a factor.

There was 37.27 % metastatic and 62.73 % localized malignancy. This value is 3 times higher than that stated in the literature [18,19] . This is highly probably due to longer time lag to consultation and diagnosis in our context.

There was a higher occurrence of associated anomalies in our study compared to the NWTS group (8.2 % in our study against 7.3 % in NWTS group) [20]. According to literature, bilateral disease occurs in 5 % of cases of NPH [19] similar to the 6.06 % we had in our study.

When it came to histology, based on the revised SIOP classification of renal tumours of childhood (2001), the most frequent histological subtypes corresponded to the intermediate risk group (20; 29.85 % mixed, 7;10.45 % stromal, 4; 5.97 % regressive, and 3; 4.48 % epithelial), followed by the high risk group (19; 28.36 % blastemal). This is similar to that stated by the Groupe franco-africain d'oncologie pédiatrique (GFAOP) [21].

The treatment of NPH largely depends on the stage. The advanced stages generally spent a longer time hospitalized. In our study, we realised that 24 (17.14 %) cases were treated with chemotherapy only, while 108 (77.14 %) with combined chemotherapy and surgery with just 5.72 % of cases who did not receive any form of treatment mostly due to death before onset of chemotherapy or rejection of diagnosis. These findings differ with that of Mwamba *et al* in Kenya who had 46.9 % of cases receive no treatment and only 37.5 % received complete therapy mainly due to the unavailability of drugs [15]. This could also be explained by the fact that the treatment for NPH in our setting is free.

20 (12.66 %) cases abandoned the treatment, 17 (10.76 %) cases witnessed a relapse, 101 (63.92 %) had remissions and 45(28.48 %) patients died. The outcomes of 12 (7.59 %) cases were otherwise not specified. These data are similar to that of kim *et al* in North America [22], with NPH having spectacular results on treatment. In our context, treatment for NPH has been subsidized, and is almost free for the patients, thus many more stick to the treatment.

The overall survival of NPH at 2 years and 5 years was 72 % and 70 % respectively. There was a gross difference in the survival rates of those who completed treatment and those who did not at 92 % versus 21 %. These results are similar to the findings of Rais *et al*, who had overall survival at 78.7 % and 70.1 % at 2 and 5-year survival respectively [14]. The treatment of NPH is increasingly becoming a success story in our setting.

### Limitations and difficulties encountered

We have achieved our goals. However, like any retrospective study, we have been confronted with some important limitations and difficulties, namely missing

data in patients' files in a context where there is no archiving system.

## CONCLUSION

Our study showed a male predominance. In our context, the Wilms tumor is a disease of the young child under 7 years old. Most came late with advanced disease. Many cases have not received treatment. The results are still poor in our context. A prospective study with a database would allow a better appreciation of the treatment of wilms tumor in Cameroon.

### Prior presentation

There has been no prior presentation.

### Author contributions

Conception and design: Angele Pondy, Kenn Chi Ndi,
Administrative support: Koki Ndombo, Angele Pondy
Provision of study materials or patients: Angele Pondy
Collection and assembly of data: Angele Pondy, Kenn Chi
Data analysis and interpretation: Angele Pondy, Kenn Chi
Manuscript writing: All authors
Review of the article: Bernadette Ngo Nonga
Accountable for all aspects of the work: All authors

### Authors' disclosures of potential conflicts of interest

The following represents disclosure information provided by authors of this manuscript. All relationships are considered compensated. Relationships are self-held unless noted.

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