

Preliminary Study of Histo-Prognostic Factors of Nephroblastoma at Thiès Regional Hospital Center

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Abstract

Introduction: Nephroblastoma is a malignant embryonic tumor developed from metanephrogenic blastema. Its treatment is multidisciplinary. The objective of our work is to study the histoprostic factors of nephroblastoma at the regional hospital of Thiès. **Materials and Methods:** This is a retrospective, cross-sectional and descriptive study of nephroblastoma over a period of 20 months, from September 22, 2022, to April 30, 2024. It was conducted in the pathological anatomy and cytology laboratory of Thiès Regional Hospital Center. Were included all children in whom nephroblastoma diagnosis was made on clinic and radiological evidence, which was confirmed by histological examination. **Results:** In total, 38 patients were eventually involved. The average age was 47 months with a female predominance. The circumstances of discovery were the abdominal mass present in 97% of cases. Thirty-seven (37) unilateral total nephrectomy specimens were recorded, with one case of bilateral nephroblastoma. The tumor predominated in the left kidney in 68 % of cases. The average tumor size was 14 cm. Regressive and mixed type nephroblastomas were the most represented cases, with 25.6% each. Intermediate risk was the most common factor, with 33 cases. Stage II was the most represented stage, and involved 17 nephrectomy specimens. **Conclusion:** The treatment of nephroblastoma in Thiès is multidisciplinary. It is a cancer that remains of late discovery in our context.

Keywords

Preliminary Study, Histo-Prognostic Factors, Nephroblastoma, Thiès

1. Introduction

Nephroblastoma or Wilms tumor (WT) represents 5 to 15% of all pediatric cancers [1]. Its pathophysiology is multifactorial and its development involves at least 10 genes, most of which are associated with family diseases or malformation syndromes [2]. The treatment of nephroblastoma is multidisciplinary, and multi-institutional clinical trials have considerably improved the survival rate. In Senegal, the treatment of nephroblastoma is only possible in a few hospitals that are in large cities [3]. It is codified by the therapeutic protocols of the Franco-African Pediatric Oncology Group (GFAOP) from the International Society of Pediatric Oncology (SIOP). These studies have defined different risk groups, which makes it possible to adapt the intensity of the treatment, thus limiting complications and treatment costs. In Thiès, activities on nephroblastoma started in September 2022 and are solely based on surgical intervention and anatomopathological examination. Pre- and post-operative chemotherapy and radiotherapy involve several specialized centers located in Dakar, the capital of Senegal. This scheme therefore requires close collaboration between pediatric surgeons and pathologists from Thiès regional hospital center, pediatric oncologists, radiotherapists and pathologists from the Reference Center for the Diagnosis of Childhood Cancers (CRDCE) located in Dakar. In this study, we report the activity record of the treatment of nephrectomy specimens for nephroblastoma in the pathological anatomy laboratory of Thiès Regional Hospital Center. As far as we know, this is the first study carried out in a decentralized area on nephroblastoma. The objective of our study is to present, through a retrospective series, the epidemiological profile, and the anatomopathological particularities of this tumor.

2. Materials and Method

This is a retrospective, cross-sectional and descriptive study over a period of 20 months, from September 1, 2022 to April 30, 2024. It was carried out from patient records collected at the pathological anatomy and cytology unit of Thiès Regional Hospital Center. Were included in the study all children aged 0 to 16 years who had surgery, with histological evidence of nephroblastoma. Other malignant tumors of children's kidney, as well as tumors awaiting immunohistochemistry were excluded. For each patient, we established an operating sheet including epidemiological data (sex, age, geographical origin), the circumstances of discovery, the results of the anatomopathological study (the nature of the sample, the location of the tumor, the structure of the tumor, the histological type, the histo-prognostic grade and the stage of tumor extension) and the evolution of patients under treatment. The initial stage of patient treatment consisted of the radiological diagnosis of nephroblastoma, the balance of extension by abdominal ultrasound, abdominopelvic computed tomography, and frontal and lateral chest X-ray. The non-metastatic character was based on the normality of the standard X-ray and the hepatic ultrasound. A complete blood count (CBC) was also performed. The preoperative chemotherapy protocols included vincristine, actinomycin D and adriamycin.

The indications were based on the localized or metastatic character. After the surgical procedure, each excision specimen was sent to the pathology laboratory in a fresh state after surgical resection. They came each with a request form for anatomopathological examination specifying the civil status, clinical information, and the surgical report. The macroscopic examination consisted in opening the specimen on the largest axis by passing through the convex edge; then cutting cross-sectional slices parallel to the major axis. The specimen was then placed in formalin for 48 H - 72 H. After the formalin fixation stage, a macroscopic examination was carried out according to the standard protocol. The inking of the excision limits had been carried out on all the specimens. Likewise, all samples had been subject to a complete section slicing on macroscopic examination. Systematically, samples of the tumor-hilum, normal tumor parenchyma and capsule kidney tumor ratios were performed on the nephrectomy specimens. As for the lumpectomy specimens, a complete section slicing was included in its entirety. After macroscopic examination, the histopathological techniques consisted of dehydration, paraffin embedding, and microtomy. Hematoxylin eosin is the coloring technique used for this. The slides were then read on an optical microscope, thus making it possible to specify the histological type and tumor extension stage. Systematically, all nephroblastoma slides read in the pathological anatomy and cytology laboratory of Thiès Regional Hospital Center had been subject to a double reading by the Reference Center for the Diagnosis of Childhood Cancers (CRDCE). The post-operative therapeutic strategy was based on chemotherapy using the same molecules as in the pre-operative phase, which was associated or not with radiotherapy. The therapeutic indications were based on the stage, histological forms and tumor volume. Data entry and analysis were carried out on Excel 2013. Quantitative variables included the mean, standard deviation and median. For qualitative variables, we made graphical representations of the numbers and frequencies.

3. Results

Thirty-eight (38) children were recorded in our series. The mean age was 47.62 months, with extremes of 1 month and 180 months. The median was 36 months. The most represented age groups were those included in the [21 - 40 months] and [41 - 60 months] interval, with 11 cases each, representing 29% of cases (**Table 1**).

Table 1. Distribution of patients by age group.

Age group (months)	Number	Percentage
[0 - 20]	9	24%
[21 - 40]	11	29%
[41 - 60]	11	29%
[61 - 80]	2	5%
[81 - 100]	2	5%

Continued

[101 - 120]	1	3%
[121 - 140]	1	3%
[141 - 160]	0	0%
[161 - 180]	1	3%
Total	38	100%

The sex ratio was 0.81. Most of the children resided in Dakar. The other children came from other regions of Senegal. One child was from Guinea Conakry (Table 2).

Table 2. Distribution of children by residence.

Geographical origin	Number (n = 38)	Percentage (%)
Dakar	12	31.5%
Thiès	5	13.16%
Diourbel	3	7.8%
Ziguinchor	3	7.8%
Kaolack	3	7.8%
Saint-Louis	2	5.26%
Louga	1	2.63%
Fatick	1	2.63%
Tambacounda	1	2.63%
Kaffrine	1	2.63%
Kolda	1	2.63%
Sedhiou	1	2.63%
Guinea Conakry	1	2.63%
Not specified	3	7.89%

Clinically, abdominal mass was the main circumstance of discovery in 37 patients, which is 97% of cases, followed by abdominal pain in 11 patients, representing 29% of cases, fever in 5 patients and hematuria in 3 patients. Other symptoms were polymicroadenopathies in 4 children, underweight in 3 children and urinary disorders in 1 child. In addition to the assessment of general condition and nutritional status on admission, the children underwent a blood count. Anemia was recorded in 32 patients; 24 children had thrombocytosis and hyperleukocytosis was present in 08 patients. The children also benefited from a preoperative imaging examination including, for the majority (36 patients), an ultrasound scan as well as an abdominopelvic CT scan. Twenty-seven (27 children) benefited from a chest X-ray. The tumor was isolated and unilateral in most cases; left-sided in 24 children and right-sided in 13 children. One (01) child presented a bilateral nephroblastoma. Pulmonary metastases were found in 08 patients. The appearance

of the tumor was variable on ultrasound, the heterogeneous forms most often associated fleshy areas, cystic areas and necrotic areas. For 08 children, the structure of the tumor had not been specified (**Table 3**).

Table 3. Tumor distribution according to structure.

Ultrasound appearance	Number	Percentage
Fleshy	13	37.14%
Heterogeneous	12	34.28%
Necrotic	1	2.86%
Cystic	1	2.86%
Not specified	8	22.86%

All our children underwent radical surgery. They were given adjuvant chemotherapy in 97% of cases (n = 37); with only one child having immediate surgery. The average number of cures was 4, with extremes from 1 to 13 cures. The samples received at the laboratory consisted of 35 pieces of unilateral total nephrectomy, and 4 pieces of lumpectomy. The renal capsule was analysed on the nephrectomy specimens. It was intact for 26 specimens, and nine (09) samples presented an area of capsular transgression. For the nephrectomy specimens, the average weight was 688 g with extremes of 78 g and 3000 g (**Table 4**).

Table 4. Distribution according to weight of nephrectomy specimen.

Weight of the nephrectomy specimen	Number	Percentage
50 - 200 g	2	5.71%
201 - 500 g	16	45.71%
501 - 1000 g	6	17.14%
1001 - 2000 g	4	11.43%
2001 - 3000 g	3	8.57%
Total	35	100%

For the lumpectomy specimens, the weight was specified in 03 patients. The average weight was 48.66 g with extremes of 5 g and 130 g.

The average tumor size on the nephrectomy specimen was 14 cm, with extremes of 7 and 26 cm (**Figure 1**). Most samples had a tumor size between 11 cm and 15 cm for a total number of 19 cases, which is 54.28% of cases (**Table 5**). Regarding lumpectomy specimens, the sizes varied from 1.5 cm to 9 cm in diameter.

A renal vein embolism was found in three (3) children. In seven (7) children, lymph node dissection was associated with the nephrectomy specimen. All the lymph nodes removed were of reactive nature, without any metastatic invasion. The number of tissue blocks averaged 21, with extremes of 2 and 65 tissue blocks. On histological examination, mixed type and regressive type nephroblastoma were predominant (**Figure 2**).

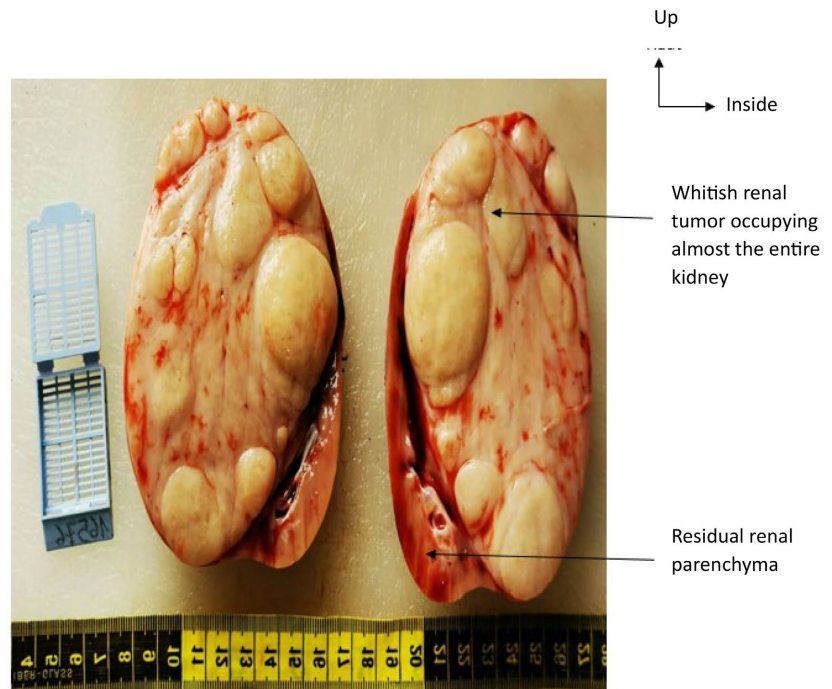


Figure 1. Total left nephrectomy for nephroblastoma. Anapath Lab. TRHC.

Table 5. Distribution according to size of nephrectomy specimen.

Specimen size	Number	Percentage
1 - 5 cm	0	0%
6 - 10 cm	8	22.86%
11 - 15 cm	19	54.28%
16 - 20 cm	4	11.43%
21 - 30 cm	4	11.43%
Total	35	100%

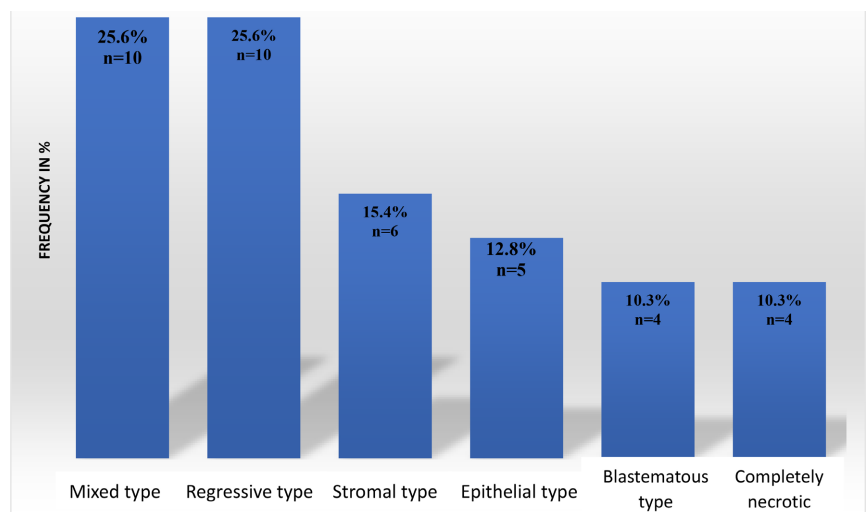


Figure 2. Distribution of nephroblastomas according to histological types.

A heterologous component was found in six (6) patients; it was adipocytic in 01 patient, rhabdomyoblastic in 04 patients and unspecified in 01 patient. According to the risk group, nephroblastoma was of intermediate risk in 32 patients, high risk in 4 patients, and low risk in 3 patients. Focal anaplasia hotspots were present in 01 child. Nephrogenic remains were present in 06 patients. The stage of tumor extension was analysed on 35 nephrectomy specimens, of which 17 specimens were classified as stage II, followed by stage III with 10 specimens and finally stage I with 08 surgical specimens. Postoperatively, thirty-five (35) children underwent chemotherapy, and 1 patient underwent radiotherapy. The use of chemotherapy for neo-adjuvant therapy was not specified in 2 children. Regarding long-term results, treatment is still ongoing in 20 patients, representing 53% of our series. Eight (8) patients were declared cured, and 08 cases of death had been recorded, which represents 21% of our sampling. Two postoperative complications were noted, which consist of a double recurrence of nephroblastoma in the first patient, and hepatic and pulmonary metastases in the other patient, which is approximately 5% of cases.

4. Discussion

Our study involved 38 children with a nephroblastoma condition confirmed by histological examination. Collected data may not reflect the situation in the general population of our region. Indeed, the selection of patients was based on the anatomopathological examination reports of Thiès Regional Hospital Center. Even if this laboratory is the only center specialized in the reading of nephroblastoma slides, the patients in our context most often resort to traditional treatments, which reduces the sample. In addition, lack of awareness of cancer is a barrier to consultation. It is therefore important that public authorities organise campaigns to raise patients' awareness on the importance of early consultation as soon as the appearance of warning signs such as abdominal deformity or urinary disorders in children. According to a previous study carried out in 2020 within the framework of the CRDCE (Reference Center for the Diagnosis of Childhood Cancers) in Dakar, nephroblastoma appears at the top of solid tumors in children [4]. In the study by Togo in Mali, nephroblastoma ranked 3rd rank in childhood cancers, with a frequency of 14.8% of cases [5]. In Europe, the data vary depending on the series. Pastore, on a European series, found a frequency of 93% on all childhood kidney cancers [6]. In France, it is estimated to be 5% of all childhood cancers, with 1 case per 10,000 births and nearly a hundred cases per year on average [7]. In Switzerland, the annual incidence is 0.8 - 0.9/100,000 [8], and Trobs in Germany reported a frequency of 94.80% [9]. The time between the appearance of the first signs and the consultation was not specified on the pathological examination sheets, which represents a limitation in our study. This delay appears to be particularly long in most African studies, reaching up to 9 months in some observations [10] [11]. The main reasons for late referral reported by the authors were parental poverty, resort to old traditional treatments, lack of adequate infrastructure, insufficient

technical facilities, lack of qualified personnel and cultural beliefs evoking witchcraft or bad luck. Nephroblastoma in our context presents clinically as a large renal tumor invading almost the entire kidney of the child, which reflects an advanced clinical stage of the disease. The tumor is then fragile and can rupture with a risk of dissemination of cancer cells. It is therefore important to identify and analyse, through further, more exhaustive studies, the potential factors influencing the diagnostic delay.

The mean age of 47.62 months in our series is similar to that of Togo in France [12] and Doumbia in Mali [1] which reported average ages of 30 months and 33 months respectively. Other studies carried out in Guinea Conakry, Japan and China reported average ages of 56.5 months [13], 2.8 years [14] and 3.1 years [15] respectively. In Switzerland as well, Diézi's series reports a mean age of 3.1 years with extremes of 0 to 13 years [8]. All these data show that nephroblastoma is truly a tumor of early childhood. The female predominance in our series is comparable to that of Togo [16] and Abuidris [17], with respective sex ratios of 0.64 and 0.9. However, Njiki, in their series, had found a male predominance with a sex ratio of 1.1 [18]. The left kidney was the preferential site in our series, with a case of bilateral nephroblastoma. Atteby [19] reported a predominance of nephroblastoma on the left side with 53% of cases on the left versus 43% of nephroblastoma on the right. As for Togo, he had found that the right-sided ailment was predominant [20]. Diakité [21] and Lancaster [22] reported an almost even distribution between the two kidneys. The same authors reported cases of bilateral nephroblastoma with 1 child and 9 children respectively.

Preoperative chemotherapy was the rule for our patients and in most series. In Suita's study, 100% of children had received primary chemotherapy [14] and in Hall G's study, preoperative chemotherapy involved 114 children, which is 71.2% of the sample [23]. The average tumor size was 14 cm, larger than the values of Pasticier who, in a French study, reported an average tumor size of 4.6 cm [24]. Histologically, the regressive and mixed type nephroblastomas, with 10 cases each, which is 25.6%, were the most frequent. In his series, Lancaster found a predominance of the blastematos type with 33.2% of cases [22]. Histological examination, the location of the cancer at the time of diagnosis and the response to preoperative chemotherapy had made it possible to classify patients according to the level of risk and the stage of tumor extension. The study of histo-prognostic factors showed a predominance of intermediate-risk nephroblastoma. This result is similar to that of Doumbia in Mali which reported 67% intermediate risk [1]. The local stage of tumor extension defined by SIOP showed a predominance of stage II, with 17 patients, or 49% of the cases in our series. A previous study carried out in Dakar showed a predominance of stage I. Stage III was more frequent in the series of Lancaster [22] and Ying Yang [15], with respective rates of 83.9% and 40%. Stages IV and V were rarely described in the literature. Lancaster [22] reported 5.95% for stage IV and 5.4% for stage V. Ying Yang [15] and Moreira [25] did not find stage V but reported stage IV patients with respective rates of 20% and 23%.

5. Conclusion

Nephroblastoma remains a kidney cancer of early childhood. Its diagnosis is revealed by the discovery of a large tumor in the abdomen region that can rupture and cause metastasis. Its treatment is multidisciplinary and codified by the SIOP protocols.

Authors' Contribution

All authors contributed to the development of the study, and have read and approved the final version of this manuscript.

Conflicts of Interest

The authors declare having no conflicts of interest.

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