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Ultra Sonographic Profile of Nephroblastoma at the University Clinics of Kinshasa

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Abstract

Objective: To describe the ultrasonographic profile of nephroblastoma diagnosed at the university clinics of Kinshasa. Materials and methods: This is a descriptive study; it concerns 45 patients with Wilms' tumor diagnosed by ultrasonography at the university clinics of Kinshasa from 2016 to 2021, i.e. an overall period of six years. Two ultrasound scanners branded Phillips u-22 and Mindray DC-30 were used. Materials and methods:This is a descriptive study; it concerns 45 patients with Wilms' tumor diagnosed by ultrasonography at the university clinics of Kinshasa from 2016 to 2021, i.e. an overall period of six years. Two ultrasound scanners branded Phillips u-22 and Mindray DC-30 were used.

Index terms— nephroblastoma, ultrasonography, pediatrics and histopathology.

1 I.

Introduction ephroblastoma, or Wilms' tumor, is a renal tumor occurring predominantly in children. It accounts for more than 90% of malignant renal tumors in children and mainly affects children under 5 years of age [1][2][3]. Nephroblastoma is very different from adult kidney cancer, as it is an embryonic tumor, developing from the metanephros, whose differentiation and proliferation give rise to the kidney [3]. In most Western populations, nephroblastoma accounts for up to 6% of all cancers diagnosed in children. In black populations in North America and Africa, the proportion is about 10% [4]. It is rarely found in adults [5,6]. In sub-Saharan Africa, nephroblastoma is among the five diseases that account for 70% of childhood cancers [7]. Although Wilms' tumor is often curable in developed countries, affected children in middle-income countries experience poor outcomes. ABDALLAH FK et al in 2001 in an analysis of survival of nephroblastoma in Kenyan patients reported a two-year event-free survival (EFS) of 34.7% 8 which contrasts with the survival rate of over 90% at 5 years in developed countries. However, thanks to the Franco-African Pediatric Oncology Group (FAOPG), a protocol adapted to the African context where patients are seen late with large abdominal masses has significantly improved the prognosis in French-speaking Africa [7,9]. Ultrasonography, plays a key role in the management of Wilms' tumor, as the decision to initiate preoperative chemotherapy is made without pathological evidence, according to the 2001 International Society of Pediatric Oncology (ISOP) protocol [2,10]. Nephroblastoma represents the third most common pediatric cancer (15%) after non-Hodgkin's malignant lymphoma and retinoblastoma according to the study carried out by ABDOUL KD et al in the Bamako pediatric oncology unit [9] in Mali. In the Democratic Republic of Congo (DRC), studies by MPUTU [11], LUNTALA [12], KONGOLO [13], PALANGI [14] and KAZADI [15] in the eighties and nineties had demonstrated that this serious pathology was frequent in our setting and posed a real problem of early diagnosis. A literature review of cases in the pediatric hemato-oncology unit of the CUK had reported between 2000 and 2018 a rate of 13% of cases of nephroblastoma, placing it in 4th position after retinoblastoma, lymphomas and leukemias [16]. Although some studies evaluating the frequency of nephroblastoma on the basis of conventional radiology data have already been carried out [10], no study to date has evaluated the contribution of ultrasonography in the management of nephroblastoma in the hospital setting of Kinshasa; hence the interest of the present study, whose mission is to describe the ultrasonographic profile of nephroblastoma in the university clinics of Kinshasa.

2 II.

3 Materials and Methods

Type and period of the study: This was a descriptive documentary study of nephroblastoma cases diagnosed in the medical imaging department of the CUK during a period of six years from January 2016 to January 2021. Study population: this study included 45 patients, aged from 1.5 months to 10 years with a median age of 3.0 with extremes (2.0-4.0) years. Thirty patients were male and 15 females. Inclusion criteria: Any patient referred for suspicion of an abdominal mass with a lumbar contact; any patient who had undergone a renal Doppler ultrasound scan; and any patient with a complete medical record. Non-inclusion criteria: The following patients were not included in this study: patients who did not perform a renal Doppler ultrasound, patients who did not perform histopathological analysis after surgery, and patients with incomplete medical records. In relation to the parameters of interest and operational definitions we noted: a) Socio-demographic parameters: including age and sex of the patients; b) Clinical parameters: including sensation of an abdominal mass with lumbar contact on palpation, hematuria, abdominal pain, altered general condition, digestive disorder and notion of abdominal trauma; c) Biological parameters: hemoglobin, urea and creatinine; d) Ultrasonographic parameters: b.1) tumor location: right unilateral, left unilateral or bilateral; b.2) the renal take-off point: (upper pole, lower pole, medio renal, toto renal); b.3) the tumor volume, obtained by automatic multiplication of the height (h) times width (l) times thickness (e) with a conversion factor of 0.523 (h x l x e x 0.523); the product is expressed in cm3 or ml; b.4) the echostructure: which can be used to determine the size of the tumor; b.5) the size of the tumor: (h x l x e x 0.523)) the echostructure: which can be solid, mixed (solid-cystic) and or cystic; b.5) the necrotic-cystic zones: defined by the presence of empty patches of echoes within the tumor mass, b.5) the presence or absence of the tumor capsule: defined by a thin layer separating the b.6) Tumor echogenicity: defined by the brightness or not of the tumor in relation to the surrounding structures, which may be hypoechoic, hyperechoic or isoechoic; b.7) Spur sign: defined by the extension of the healthy renal parenchyma progressively connecting to the renal mass (fig. **??**1), b.8) Contours: defined by the limits of the tumor and can be regular or irregular; b.9) Tumor rupture: defined by the presence of a perirenal or peri-tumoral collection, b.10) Calcifications: defined by the presence of intra-tumoral hyperechoic images with or without posterior shadow cone, b.11) displacement of the pyelocal cavities and/or vessels: defined by the displacement of intra-abdominal organs adjacent to the tumor, b.12) compensatory hypertrophy of the contralateral kidney: defined by an increase in size of the breast kidney, b.13) tumor vascularization (fig. 12), b.14) loco-regional tumor extension: defined by the invasion of loco-regional structures by the tumor; the latter may be: the renal vein and or the inferior vena cava by a thrombosis (fig. 12), the transmedian extension; defined by the overtaking of the median line by the tumor, the latter defined by the linea alba, the intraperitoneal effusion by an attack on peritoneal, the satellite nodule on the homolateral or contralateral kidney, adenomegaly (fig. 13), and finally hepatic nodules. e) The anatomopathological parameters sought were: e.1) the histological type of the tumour: (mixed, stromal, epithelial and blastematous), e.2) risk and stage according to the 2001 SIOP classification, and e.3) grouping of four stages into two main groups: stages I and II: considered as tumors with complete resection and stages III and IV considered as tumors with incomplete resection according to the ultrasonographic characteristics. As for data processing and statistical analysis, it should be noted that the data were collected on a collection form encoded using Excel 2013 software. After verification and cleaning of the database, they were exported to SPSS for Windows version 24 for analysis. Categorical variables were presented as absolute and relative frequencies (%), quantitative variables were summarized by measures of central tendency and dispersion. The mean and its standard deviation were reported for data with a Gaussian distribution; however, those that did not follow the Gaussian distribution were summarized as median and interquartile range (IQR). Pearson's chi-square or Fischer's exact test was used to compare proportions; Student's t-test compared means; and Mann Whitney Utest compared medians. For all tests used, the p value ? 0.05 was the threshold of statistical significance.

4 III.

5 Results

In relation to sociodemographic parameters; the median age in the present study was three years with the extremes ranging from two months to ten years [Figure **??**]. The majority of patients were between two and four years of age (44.4%) [Figure **??**]. The majority of patients were male (66.7%) with a sex ratio of 2:1 [Figure **??**]. Median urea and creatinine values were 20.8 (13.4-27.1) mg/dl for urea and 0.60 (0.45-0.70) mg/dl for creatinine. The overall mean hemoglobin value was 8.5±1.9 g/dl [Table 1]. Ultrasonography, was used in forty-five patients, or 100.0%. We noted twenty-two tumors in the left kidney, or 48.88%, nineteen tumors in the right kidney, or 42.22%, and bilateral localization in two patients, or 4.44% [table 2]. The majority of tumors presented a solid, heterogeneous echostructure in twenty-four patients, i.e. 53.33%; solid tumors with necrotic-cystic patches were present in nineteen patients, i.e. 42.22% [Table 2]. In relation to flight points: nineteen tumors were upper polar or 42.22%, eleven lower polar tumors or 24.44%, one mid-polar tumor or 2.22% and twelve total renal tumors or 26.66% [Table 2]. The median value of tumor volume was 985 (665-1196) ml with the extremes ranging from 100 ml to 6127ml. Spur sign was found in twelve patients or 26.66%. The tumor contours were irregular in thirty patients or 66.66% and regular in thirteen patients or 28.88% % [Table 2]. The tumor capsule was intact in

eighteen patients, or 17.77%, while tumor rupture was found in three patients, or 6.66% [Table 2]. The pyelocalic cavities were repressed in four patients, or 8.88% [Table 2]. In relation to tumor echogenicity, there were twenty-three hypoechoic tumors, or 51.11% [Table 2]. In boys, twelve patients or 42.9% had hypoechoic tumors, whereas in girls eleven patients or 73.33% had hypoechoic tumors [Table 1-2]. Hyperechoic tumors were found in twelve patients, i.e. 26.66%; in boys nine patients, i.e. 32.1% and in girls three patients, i.e. 20% and iso echogenic tumors in eight patients of which seven boys and one girl. We found intra-tumor calcifications in nine patients, or 20% [Table 2]. Compensatory hypertrophy of the contralateral kidney was found in four patients, i.e., 8.88%, and tumor vascularization was well objectified in seventeen patients, i.e., 37.77% [Table 2]. The inventory of the parameters of locoregional tumor extension on ultrasonography reveals the following; reflow without invasion of neighboring structures was found in seventeen patients, i.e., 37.77%; adenomegaly was found in thirteen patients, i.e., 28.88% [Table 2]. Venous thrombus was found in twelve patients, i.e. 26.66%, in five patients, i.e. 11.11%, the thrombus was located within the renal vein and in seven patients, i.e. 15.55%, the thrombus was located within the inferior vena cava [Table 2]. In seven patients (15.55%), we found a transmedian extension [Table 2]. Peritoneal fluid effusion was found in five patients (11.11%) and liver metastases in three patients (6.66%). The whole group had a median tumor volume of 560.6 (313.9-843.4) ml [3]. We noted 85.7% of tumors of intermediate risk against 7.1% of low and high-risk tumors in the same proportions [Figure **??**].

6 IV.

7 Discussion

In our series, the median age in the study population was 36 months with the extremes ranging from 2 months to 120 months. The majority of patients were between 2 and 4 years of age, representing 44.4% of cases. Diakité F et al [17] and Atanda AT et al [18] respectively in Guinea (2012) and Nigeria (2015) had found a mean age of about 5 years. Age extremes ranging from 13 to 130 months in the study of Diakité et al [17]. This difference could be explained by the improved management with the support of GFAOP. Molua, in his final thesis, found extremes of age from 12 to 60 months [1]. This statement is consistent with our observation and those of several authors [2,9,10,19]. In the present study, the male sex was the most affected with a sex ratio of 2/1. Kanté A. et al [20] had noted a slight female predominance. Our observation is similar to those of Atanda AT et al [18] and Diakité F. et al [17]; however, no statistically significant association has been demonstrated. In our series, the clinical signs were dominated by the discovery of abdominal distension (71.1%), followed by general signs (44.4%), abdominal mass with lumbar contact (35.6%), abdominal pain (31.1%), hematuria (24.4%), constipation (2.2%) and trauma (2.2%). These results are consistent with those of Bouzhir AM et al [21]. according to data from the National Cancer Institute in the USA [21]: asymptomatic abdominal distension: is the most frequent clinical presentation found in children during bathing or dressing. Abdominal pain is seen in 40% of cases; macroscopic hematuria in 18%, microscopic hematuria in 24% and hypertension present in almost 25% of patients at the time of discovery of nephroblastoma. The latter is secondary to activation of the renin-angiotensinaldosterone system. Symptoms of alteration of the general state, namely: anorexia, weight loss and fever may occur in less than 10% of cases. Other manifestations related to complications may also be indicative of nephroblastoma, including vascular obstruction, distant metastases that may be pulmonary or hepatic, pulmonary embolism, collateral venous circulation, and varicocele due to obstruction of the inferior vena cava. Renal function studied by urea and plasma creatinine was normal in our study. This could be explained by the unilaterality of the renal involvement. Indeed, in case of unilateral damage, we think that the remaining healthy renal parenchyma could contribute to the preservation of the function. These data agree with those of Molua [1] and those of the literature. Our study did not find any association with congenital malformations or genetic predisposition syndromes to nephroblastoma. This could be explained by the absence of genetic testing in patients with nephroblastoma in our series. In our series, abdominopelvic Doppler ultrasound was performed in 100.0% of patients. It found a right renal location in 19 patients (42.22%), a left renal location in 22 patients (48.88%), i.e. a unilateral involvement of 91.10%, and a bilateral involvement in four patients, i.e. 8.89%. Bouzhir MA et al [21] note that abdominal ultrasound performed in all patients (100% of cases) showed a slight predominance of right renal tumors, i.e. 50% and left renal tumors 46.7% of cases; while bilateral involvement 3.3% of cases. Our observations are similar to those of Diakité F. et al [17]. In our study, the majority of tumors had a solid and heterogeneous echostructure in 55.8% of patients. In some previous studies (LAIGLE V. et al in Nantes in 2011), tumor heterogeneity on ultrasonography represented a discriminating feature, nephroblastoma being more heterogeneous than other renal tumors; however, this feature remains at the limit of significance (p=0.05) and this was not confirmed on ultrasonography. In relation to the flight point in the present series, 19 cases (44.2%) were superior polar, 11 cases (25.6%) inferior polar, i.e. a frequency of 69.8% of polar development, 1 case (2.3%) medial-renal and 12 cases (27.9%) occupied the entire renal parenchyma. According to the literature, nephroblastoma usually develops at one renal pole but can also be multifocal, disorganizing and displacing normal anatomical elements of the kidney [23,24]. In the present study, the spur sign accounted for 27.9% (12cases). Zrig A. et al [25] in Tunisia in 2014 had found the spur sign in 45 patients out of 113 observations or 39.8%. This low rate can be attributed to the large tumor volume at tumor discovery in our series. In most cases, the mass is well limited [23]. In our series, we found masses with irregular contours in 69.8%. This high rate of irregularity of the contours could be justified by the initial ultrasound performed at an advanced stage of the tumor. The mass may appear encapsulated [23],

in our series we found 41.9% (18 cases) of encapsulated tumor and this could be related to the local stage of the mass (stage I and II and III) which is determined after nephrectomy and histopathological analysis. Most of the tumors were hypoechoic in 53.5% (23 cases), hyperechoic tumors in 27.9% (12 cases) and iso echogenic in 18.6% (8 cases); hypoechoic masses were more noticed in girls, hyper and iso echogenic more noticed in boys with a significant statistical analysis (p=0.037) However, this data is subject to the small sample size of our study, thus opening up a boulevard for future research that may confirm or refute this hypothesis. Calcifications are possible in renal tumors but not very frequent. They are associated with the corbelling sign, invasion of the medullary canal and forward displacement of the aorta; thus posing a problem of differential diagnosis with neuroblastoma [2]. In our series, we found nine lesions with calcifications (20.9%), thus arguing in favor of an advanced stage tumor (III or IV); with possibility of incomplete resection at surgery and significant statistical analysis (p=0.001). In relation to locoregional extension: venous thrombosis is classically described as a sign pointing to a nephroblastoma. In our series, we found 12 patients with venous thrombosis, i.e. 26.66%; among them, 5 patients, i.e. 41.66%, had benefited from a histopathological analysis after nephrectomy, the diagnosis of nephroblastoma was confirmed. LAIGLE et al [2] found 4 cases of nephroblastoma, two of tumors were non-nephroblastoma, 6 cases (10%) out of 60 and the 2 cases were false negative on ultrasound and thrombosis present on CT. The high rate of venous thrombosis in this study could be justified by the late discovery of the tumor on the one hand and by the ability of the radiologist to look for it before any case of nephroblastoma on the other. According to the literature [2], it is known that large nodes can be found in reaction to the tumor, without tumor invasion. Their presence may be responsible for false positive lymph node metastases. During the operation, the surgeon has no intraoperative morphological criteria to differentiate metastatic adenopathy from reactionary adenopathy. Only histological data can be used to determine this difference, which is why the SIOP recommends systematic lymph node biopsies. However, their absence could be reassuring as to the lymph node status. In our series, we found thirteen patients (28.88%) with adenomegaly of which ten patients had undergone nephrectomy and histopathological analysis which showed six patients with completely resected tumors (i.e. stage I and II) and four patients with incompletely resected tumors (i.e. stage III and IV) and the difference was statistically insignificant (p=0.609), justifying that any adenomegaly would not mean tumor invasion. In our series, we found patients with metastasis in 17.7% or eight patients. Metastases were localized only to the lungs in five patients and to the liver in two patients. The simultaneous localization of the liver and lung in one patient, i.e. a hepatic localization in 37.5% of the metastatic patients, this high rate of liver metastases could be justified by the late discovery of the tumor. In the literature, liver metastases are much rarer [10]. KADRI N. et al in Morocco in 2021 **??**37], found three patients with liver metastases out of thirteen metastatic patients, i.e. a proportion of 23%. These three cases had simultaneous metastases in the lung. MOULOT MO et al [19] in Ivory Coast 2018 had found metastatic cases in 18.6% (n = 10). Chest X-ray was performed in all patients i.e. 100% to look for lung metastasis. In this study 64.4% (n=29) of patients had undergone histological analysis after extended nephrectomy. All patients had benefited from histology in the studies conducted by LAIGLE V and MOLUA [1,2]. This low rate of histology in our series could be explained by the lack of financial means for some parents, the absence of surgery for some patients, the non-availability of the histological report in the patient's file and death before a possible nephrectomy. However, this cohort remains representative with figures usually described, with a clear predominance of nephroblastoma, representing 93.1% (27 cases) in this series, the figures in the literature range from 87 to 93% [1,2,10,23]. In our study, a large majority of patients presented with intermediate risk tumors at 85.7%, whereas FOFANA N.S et al [22] found 62.5% of high-risk tumors. This difference could be explained by the fact that in the latter study only metastatic nephroblastoma's are concerned. Our study is similar to that of BOUZHIR M. A et al [21] and KADRI N. et al [26] who noted a predominance of tumors of intermediate risk respectively of 83.3% and 45%. Concerning the ultrasonographic characteristics of the renal tumors according to the clinico-pathological stage; the right location, the regular tumor contours and the spur sign were more associated with tumors with complete resection, whereas the left location, the irregular contours as well as the intra-tumoral calcifications were associated with tumors with incomplete resection with statistically significant analyses for laterality (p=0.021), contours (p=0.014), calcifications (p=0.001). The spur sign did not show a statistically significant analysis (p=0.132) but there were eight cases or 50% of completely resected tumors versus 2 cases or 20% of incompletely resected tumors. Elements such as reflow without invasion of neighboring structures and pleural effusion pleaded in favour of an incompletely resected tumour but were not statistically significant (p=0.092 and p=0.142). However, these results are taken with reservation, and we hope to carry out a study with a larger sample to confirm or refute these data. Regarding the limitations of this study, it should be noted that its retrospective nature, the lack of systematic histopathological analysis in all patients, the low rate of CT scan and the lack of nephrectomy in some patients were the main limitations of this study. As strengths: the present series, is a first study performed in our setting and having used cross-sectional imaging (US and CT).

V.

8 Conclusion

This study, which aimed to establish the ultrasonographic profile of nephroblastoma at the university clinics of Kinshasa, allowed us to make the following observations: children under 5 years of age, predominantly male, with a median age of three years, were referred for abdominal bloating, moderate anemia with disturbance of renal function; in whom abdominal palpation revealed an abdominal mass with positive lumbar contact.

The ultrasonography performed in all patients with good histopathological correlation showed the following characteristics a predominance of the left renal localization, of a solid, hypoechoic, heterogeneous tumor, with a median tumor volume of 560.6 (313.9-843.4) ml, dotted with necrotic-cystic patches, with as the most frequent upper polar take-off point, a less frequent spur sign, tumor contours frequently irregular in more than half of the patients, less frequent capsular rupture, less frequent compensatory hypertrophy of the contralateral kidney, less frequent intra-tumor vascularization, frequent repression of neighboring organs; Thrombotic impregnation was found in a quarter of patients; peritoneal fluid effusion, adenomegaly and liver metastases were less frequent. On the anatomopathological level, the mixed type was the most frequently encountered, followed by the stromal and regressive types; stages I and III were in the majority and nearly 90% of patients represented the intermediate risk. In view of the above, ultrasonography represents the imaging means adapted to the socioeconomic conditions of our population for the initial diagnosis, the assessment of locoregional and distant extension without forgetting the follow-up of the children having benefited from chemotherapy and surgery.

9 VI. Protection of Human and Animal

Rights The authors declare that this study did not involve experiments on patients, subjects, or animals. Confidentiality of Data: The authors declare that this study does not contain any personal data that could identify the patient or subject. Funding of the Study This study did not receive specific funding from any public or private institution.

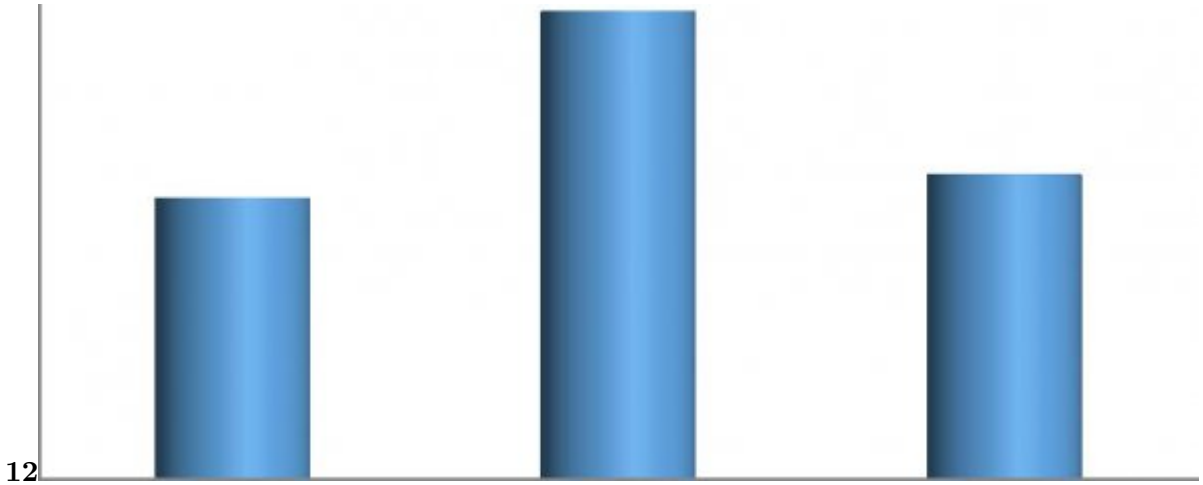

Figure 1: Figure 1 :Figure 2 :

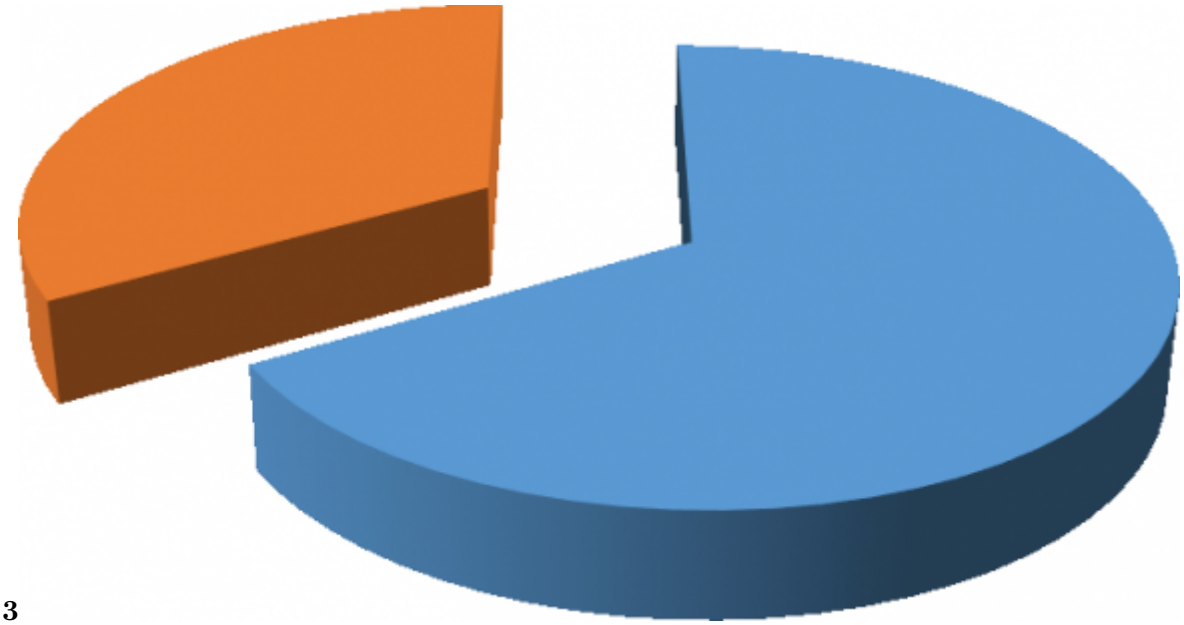

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Figure 2: Figure 3 :

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Figure 3: Figure 4 :Figure 5 :

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Figure 4: Figure 6 :

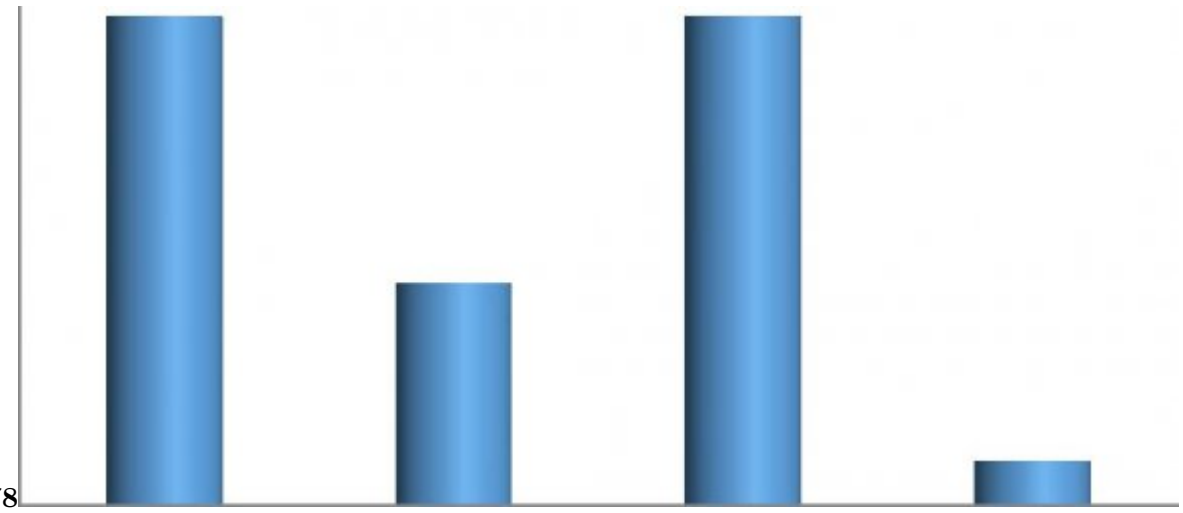

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Figure 5: Figure 7 :Figure 8 :

2

patients, or 64.4%
histopathological examination after enlarged total uretero-nephrectomy, among which we note seventeen boys or 58.62% and twelve girls or 26.66% [table 5]. According to the histological types, sixteen patients, i.e. 55.17%, presented the mixed type; the stromal and regressive types were found in 3 patients, i.e. 10.34% each; the blastomatous and epithelial types were found in 2 patients each, i.e. 6.89% [Table 5]. We also found one
nephroblastoma (3.44%) [

]. On the anatomopathological level two
had benefited from
case of partially differentiated cystic

Figure 6: Table 2

5

Figure 7: Table 5]

1

	Parameters	Whole group n=45	Male n=30	Female n=15	P
	Abdominal distension	32(71,1)	22(73,3)	10(66,7)	0,447
Year	Palpated abdominal	16(35,6)	11(36,7)	5(33,3) 5(33,3)	0,548
2023	mass Hematuria	11(24,4)	6(20,0)		0,266
6	Abdominal pain	14(31,1)	9(30,0)	5(33,3)	0,539
	General signs	20(44,4)	14(46,7)	6(40,0)	0,460
	Digestive disorder	1(2,2)	0(0,0)	1(6,7)	-
	Notion of trauma	1(2,2)	1(3,3)	0(0,0)	-
	Urea (mg/dl)	20,8(13,4-27,1)	20,5(11,9-29,3)	21,0(10,2-28,0)	0,664
	Créatinine(mg/dl)	0,60(0,45-0,70)	0,59(0,40-0,70)	0,60(0,40-0,70)	0,311
	Hb(g/dl)	8,5±1,9	8,8±1,9	8,9±2,0	0,879

Figure 8: Table 1 :

2

Variables	Total resection tumor n=16	Incompletely resected tumor n=10	P
o Clinical-pathological stages			
Tumor location			0,021
Right kidney	11(68,8)	2(20,0)	
Left kidney	5(31,3)	8(80,0)	
Echostructure			0,412
Solid	10(62,5)	5(50,0)	
Mixed	6(37,5)	5(50,0)	
Flight point			0,503
Superior pole	9(56,3)	4(40,0)	
Lower pole	5(31,3)	3(30,0)	
kidney toto	2(12,5)	3(20,0)	
Spur sign	8(50,0)	2(20,0)	0,132
Contours			0,014
Irregular	7(43,8)	7(70,0)	
Regular	9(56,3)	3(30,0)	
Presence of the tumor capsule	8(50,0)	5(50,0)	0,656
Tumor rupture (suspicion)	0(0,0)	1(10,0)	

Figure 9: Table 2 :

3

Variables	Actual number	Percentage
o Histological type of tumors		
Mixed type nephroblastoma	16	55,2
Nephroblastoma, stromal type	3	10,3
Nephroblastoma, régressive type	3	10,3
Nephroblastoma blastematous type	2	-
Nephroblastoma epithelial type	2	-
Inflammatory mass	1	-
Partially cystic differentiated nephroblastoma	1	-
Mesoblasticnephroma	1	-
Total	29	100,0
o Tumor risk		
Intermediate Risk		85,8
High risk		7,1
Low risk		7,1
Total		100

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Figure 10: Table 3 :

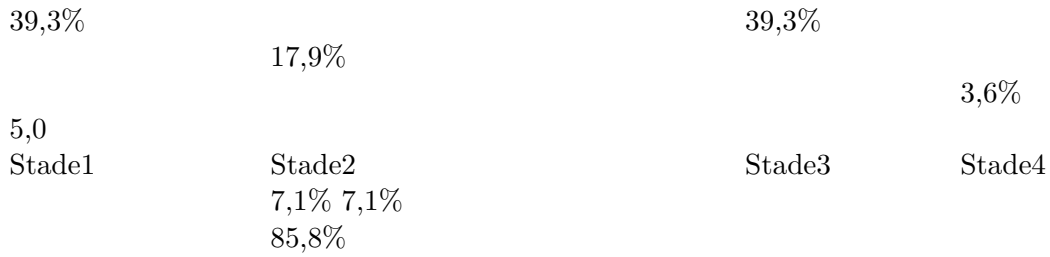

Figure 11: Low risk Intermediate risk High risk

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