American Journal of Medicine and Medical Sciences 2025, 15(11): 3789-3795
DOI: 10.5923/j.ajmms.20251511.08

Prognostic Significance of Immunohistochemical Markers in Wilms Tumor in Children

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Abstract **Relevance.** Wilms tumor remains one of the leading causes of cancer-related mortality in early childhood. Immunohistochemical markers may potentially improve risk stratification and prognostication, but their clinical significance remains uncertain. **Objective.** To assess the prognostic value of CD34, Ki-67, and p53 expression in pediatric Wilms tumor in relation to recurrence, metastasis, and overall survival. **Materials and Methods.** A retrospective study was conducted involving 91 children with histologically confirmed Wilms tumor treated at the Republican Specialized Scientific-Practical Medical Center of Oncology and Radiology (RSSPMCOR) from 2015 to 2022. Epidemiological, morphological, therapeutic, and immunohistochemical data (CD34, Ki-67, p53) were analyzed. Pearson's χ^2 test, Kaplan–Meier method, and log-rank test ($p < 0.05$) were used for statistical evaluation. **Results.** A significant association was found between tumor stage and histological differentiation ($\chi^2 = 101.7$; $p < 0.00001$). Poorly differentiated tumors (G3) were more frequently detected at advanced stages. The prognostic significance of CD34, Ki-67, and p53 for recurrence and metastasis was not statistically confirmed. Overall 5-year survival was $85.6 \pm 6.3\%$. A trend toward poorer outcomes was observed in patients without IHC assessment. **Conclusion.** Although CD34, Ki-67, and p53 did not demonstrate independent prognostic significance, the absence of their evaluation was more often associated with unfavorable outcomes, highlighting the need to include IHC in the diagnostic standard.

Keywords Wilms tumor, Children, Immunohistochemistry, CD34, Ki-67, p53, Survival, Recurrence, Metastasis, Prognosis

1. Introduction

Nephroblastoma (Wilms Tumor) is the most common malignant kidney tumor in children, accounting for approximately 6–8% of all malignant neoplasms in pediatric oncology [3,6]. The incidence of nephroblastoma ranges from 8 to 10 cases per million children per year, with a peak occurrence between the ages of 2 and 4. In developed countries, survival rates can reach up to 90% with early diagnosis and appropriate comprehensive treatment [1], while in resource-limited settings, survival remains significantly lower due to delayed detection, lack of diagnostic infrastructure, and non-compliance with international treatment protocols [7].

The clinical course of nephroblastoma is often asymptomatic in its early stages, which contributes to a high proportion of advanced cases. In most instances, the tumor is discovered incidentally during abdominal palpation by parents or pediatricians. Standard diagnostic methods are based on ultrasound imaging, CT or MRI scans, followed by histological confirmation after nephrectomy or biopsy. Morphologically, nephroblastoma is a triphasic tumor consisting of blastemal, epithelial, and stromal components, though the histological presentation can vary greatly, necessitating additional stratification [5,10].

One of the promising directions in the diagnosis and prognosis of nephroblastoma is **immunohistochemical (IHC) analysis**, which enables the assessment of the tumor's molecular and biological characteristics. Among the most studied markers are:

- **WT1**, involved in kidney development and nephron differentiation;
- **p53**, which plays a key role in apoptosis regulation;
- **Ki-67**, indicating proliferative activity; and
- **CD34**, a marker of angiogenesis.

Studies suggest that high Ki-67 expression may correlate with aggressive tumor behavior and reduced sensitivity to chemotherapy [8] (Yalçın et al., 2014), while **TP53 mutations** associated with disrupted p53 protein expression are linked to poor prognosis and an increased risk of relapse [9]. **CD34**, as an indicator of microvascular density, is being investigated for its prognostic value and potential role in therapeutic response, although its significance remains debatable (Yalçın et al., 2014).

Despite therapeutic advances — including preoperative chemotherapy (within SIOP protocols) and risk-adapted

Received: Sep. 17, 2025; Accepted: Oct. 12, 2025; Published: Nov. 6, 2025
Published online at http://journal.sapub.org/ajmms

treatment strategies (as per COG guidelines) — challenges persist in risk stratification and treatment personalization. Not all IHC markers have yet been adopted in clinical practice, despite accumulated evidence of their potential prognostic importance. In settings with limited access to molecular diagnostics, it is particularly critical to identify a minimal panel of diagnostic markers that can enhance the accuracy of stratification and prognostication.

The five-year survival rate for nephroblastoma in countries with high-quality healthcare systems ranges from 85–92% [4,6]. However, in cases of late detection, anaplastic forms, or metastatic disease, survival drops to 50–60% or lower. **Early diagnosis and comprehensive morpho-immunohistochemical verification** remain the key factors determining favorable outcomes, enabling the selection of individualized therapeutic pathways [5].

Thus, in the current context, there is an increasing need for comprehensive diagnostics of nephroblastoma that necessarily includes immunohistochemical (IHC) profiling. This approach not only refines the morphological characterization of the tumor but also improves prognostic accuracy and therapeutic efficacy. The present study aims to analyze the clinical, morphological, and immunohistochemical features of nephroblastoma in children at the Republican Oncology Center, with a specific focus on identifying prognostic markers and survival-related factors.

Study Objective

To evaluate the clinical, morphological, and immunohistochemical characteristics of nephroblastoma in children and to determine the prognostic significance of CD34, Ki-67, and p53 expression in relation to tumor recurrence, metastatic spread, and overall survival.

2. Materials and Methods

This study was conducted in a retrospective design and is based on the analysis of clinical, morphological, demographic, and immunohistochemical data from 91 patients with histologically confirmed nephroblastoma who received treatment at the Republican Specialized Scientific and Practical Medical Center of Oncology and Radiology (RSSPMCOR) and its regional branches between 2015 and 2022.

Inclusion criteria for the study were: patient age under 15 years at the time of diagnosis, presence of histologically verified nephroblastoma, completion of a full course of comprehensive treatment (surgical intervention in combination with chemotherapy and/or radiotherapy), and availability of complete clinical and diagnostic documentation sufficient for further analysis.

Exclusion criteria included: absence of morphological verification of the diagnosis, presence of other malignant neoplasms, insufficient medical documentation, refusal of treatment or deviation from approved protocols, as well as age over 15 years.

Within the framework of the analysis, the following parameters were studied: patient age and sex, duration of anamnesis before medical consultation, nature of clinical symptoms, tumor localization, disease stage according to the TNM system and clinical classification, degree of histological differentiation of the tumor, volume and type of surgical intervention, sequencing and structure of the treatment provided, and presence of recurrence or metastatic spread of the disease.

Morphological verification of the diagnosis was carried out based on standard histological sections stained with hematoxylin and eosin. If necessary, **immunohistochemical (IHC) analysis** was performed using the markers CD34 (angiogenesis), Ki-67 (proliferation), and p53 (tumor suppressor), in accordance with international standards, with visual and semi-quantitative assessment of expression.

Tumor classification and staging were performed in accordance with the current recommendations of the **World Health Organization (WHO)** and the **TNM classification** of malignant neoplasms.

Statistical analysis of the data was carried out using methods of descriptive and analytical statistics. The **Pearson chi-square (χ^2) test** was used to compare categorical variables. For survival analysis, the **Kaplan–Meier method** was applied, and differences between subgroups were assessed using the **log-rank test**. The critical level of statistical significance was set at $\mathbf{p < 0.05}$.

3. Study Results

An analysis of the clinical, morphological, and therapeutic characteristics of patients with nephroblastoma revealed several statistically significant patterns related to age and sex distribution, tumor staging, degree of differentiation, and correlations between treatment regimens and the risk of recurrence or disease progression. The key findings below reflect the structure of the sample and reliable relationships between the parameters studied.

Among the 91 patients with nephroblastoma treated at the Republican Specialized Scientific and Practical Medical Center of Oncology and Radiology (RSSPMCOR), the predominant majority were children under the age of 3 — accounting for 66.0% (n = 60). This finding reflects the typical epidemiological pattern of this malignancy, which most frequently manifests in early childhood. Patients older than 3 years made up the remaining 34.0% (n = 31) of the cohort, which is also consistent with well-known clinical and statistical data on the age distribution of nephroblastoma.

The gender composition of the study cohort showed a slight predominance of females: 56.0% (n = 51) were girls, while 44.0% (n = 40) were boys. However, the χ^2 test revealed no statistically significant differences in gender distribution, either in the overall sample or when stratified by age groups ($\chi^2 = 0.00$; $p = 1.00$). These results indicate no gender-specific predisposition to nephroblastoma in this cohort, supporting the widely accepted notion that children of both sexes are equally susceptible to this type of tumor.

Analysis of Tumor Stage and Histological Differentiation

The distribution of patients by clinical stage of the tumor and degree of histological differentiation is presented in **Table 1**. The largest proportion of patients were diagnosed with **stages 2B and 3A**, each accounting for **27.5% (n = 25)**, indicating an intermediate clinical course of the disease. **Stages 3B and IV** were diagnosed in **15.4% (n = 14)** and **13.2% (n = 12)** of patients, respectively, reflecting the presence of regional (3B) or distant (IV) metastases. **Early stages (1A and 1B)** were much less frequent, occurring in only **5.5% (n = 5)** of cases. In **six cases (6.6%)**, the stage was not determined, likely due to incomplete diagnostic information.

With regard to **tumor differentiation**, high-grade malignancies predominated: **Grade G3** was observed in **34.1% (n = 31)** of patients, **G1** in **29.7% (n = 27)**, and **G2** in **27.5% (n = 25)**. Grade **Gx** (undetermined) was recorded in only **1 case (1.1%)**, and in **6 cases (6.6%)**, the degree of differentiation was not specified.

The **χ^2 analysis** revealed a **statistically significant association** between clinical stage and tumor differentiation grade (**$\chi^2 = 101.7$; df = 42; p = 0.000002**). This indicates a reliable correlation between clinical progression of the disease and morphological deterioration in tumor cell differentiation. Specifically, **G1 and G2 tumors were more commonly detected in early stages**, while **G3 tumors predominated in stages 3B and IV**, confirming a trend of decreasing cellular maturity with advancing disease.

Evaluation of the Prognostic Significance of Immunohistochemical Markers

As part of this study, an assessment was conducted to evaluate the prognostic significance of the immunohistochemical markers **CD34**, **Ki-67**, and **p53** in the context of tumor recurrence. The aim of the analysis was to identify a potential relationship between the expression of these markers and the occurrence of relapse following primary treatment. Summary data are presented in **Table 2**.

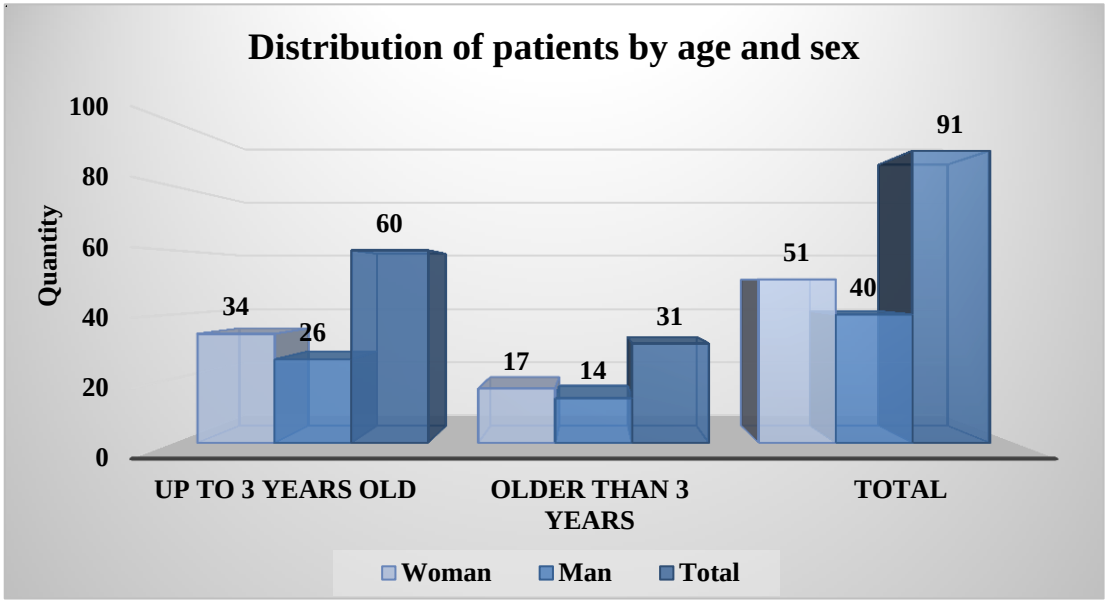

Figure 1. Distribution of patients by age and gender categories

Table 1. Distribution of patients by clinical stage of the tumor process and tumor differentiation grade

Clinical stage	G1	G2	G3	Gx	Degree of differentiation	No data	Total
Stage 1A – G1,2 T1a,бM0	1 (1.1%)	0	0	0	0	0	1 (1.1%)
Stage 1 B – G1,2 T2a,бM0	3 (3.3%)	1 (1.1%)	0	0	0	0	4 (4.4%)
Stage 2A – G3,4 T1a,бM0	1 (1.1%)	2 (2.2%)	1 (1.1%)	0	0	0	4 (4.4%)
Stage 2B – G3,4 T2aM0	6 (6.6%)	11 (12.1%)	8 (8.8%)	0	0	0	25 (27.5%)
Stage 3A – G3,4 T2бM0	7 (7.7%)	7 (7.7%)	10 (11.0%)	1 (1.1%)	0	0	25 (27.5%)
Stage 3B – G1,2,3,4 T1-2N1	7 (7.7%)	3 (3.3%)	4 (4.4%)	0	0 (0.0%)	0	14 (15.4%)
Stage IV – G1,2,3,4 T1-2M1	2 (2.2%)	1 (1.1%)	8 (8.8%)	0	1 (1.1%)	0	12 (13.2%)
No data	0	0	0	0	5 (5.5%)	1 (1.1%)	6 (6.6%)
total	27 (29.7%)	25 (27.5%)	31 (34.1%)	1 (1.1%)	6 (6.6%)	1 (1.1%)	91 (100.0%)

CD34. Expression of the CD34 marker was detected in **51 patients (56.0%)**, while in **40 patients (44.0%)**, the test was not performed. Among those with positive CD34 expression, **3 cases of recurrence (3.3%)** were recorded, compared to **5 cases (5.5%)** in the group without CD34 testing. The results of the χ^2test (χ^2**= 0.54; p = 0.4632; df = 1**) did not confirm a statistically significant association between CD34 expression levels and risk of recurrence. Thus, in this cohort, the tumor's vascular component did not demonstrate prognostic relevance.

Ki-67. A high proliferative index (≥30%) was observed in **33 patients (36.3%)**, with **1 case of recurrence (1.1%)**. Moderate expression (15–30%) was found in **7 patients (7.7%)**, with **no recorded recurrences**. Complete absence of Ki-67 expression was documented in **11 patients (12.1%)**, including **2 recurrence cases (2.2%)**. The highest number of recurrences (**n = 5**) occurred in the group where Ki-67 was not assessed (**n = 40; 44.0%**). Despite variations between groups, no statistically significant correlation between Ki-67 expression levels and recurrence rate was found (χ^2**= 3.94; p = 0.2684; df = 3**).

p53. The p53 marker was not evaluated in **40 patients (44.0%)**, of whom **5 (5.5%)** experienced recurrence. Among the rest, expression was limited: **<30%** in **16 patients (17.6%)** with **1 recurrence**, and **<50%** in **35 patients (38.5%)** with **2 recurrences**. Statistical analysis (χ^2**= 1.23; p = 0.5411; df = 2**) did not identify a significant association between p53 expression levels and the development of recurrence.

Assessment of Metastatic Status in the Context of Tumor Molecular Characteristics

Evaluating metastatic status in the context of tumor molecular characteristics is of key interest for prognostic stratification in patients with nephroblastoma. To this end, our study conducted a cross-analysis of immunohistochemical (IHC) data — including the expression of **CD34, Ki-67, and p53** — in relation to the presence of metastases.

Table 2. Distribution of patients based on the expression of CD34, Ki-67, and p53 markers and the presence of tumor recurrence

status	Recurrence: present	ecurrence: none	Total
CD34 Expression			
Not performed	5 (5.5%)	35 (38.5%)	40 (44.0%)
gender	3 (3.3%)	48 (52.7%)	51 (56.0%)
Ki67 Expression			
High (30% and above)	1 (1.1%)	32 (35.2%)	33 (36.3%)
Not performed	5 (5.5%)	35 (38.5%)	40 (44.0%)
Negative	2 (2.2%)	9 (9.9%)	11 (12.1%)
"Moderate (15–30%)	0 (0.0%)	7 (7.7%)	7 (7.7%)
P53 Expression			
<30%	1 (1.1%)	15 (16.5%)	16 (17.6%)
<50%	2 (2.2%)	33 (36.3%)	35 (38.5%)
no	5 (5.5%)	35 (38.5%)	40 (44.0%)
total	8 (8.8%)	83 (91.2%)	91 (100.0%)

Table 3. Relationship between the expression of immunohistochemical markers and the presence of metastatic disease in patients with nephroblastoma

status	**Metastases: present**	Metastases: absent	No data	total
CD34 expression				
Not performed	12 (13.2%)	27 (29.7%)	1 (1.1%)	40 (44.0%)
Gender	12 (13.2%)	38 (41.8%)	1 (1.1%)	51 (56.0%)
Ki-67 expression				
High (30% and above)	7 (7.7%)	25 (27.5%)	1 (1.1%)	33 (36.3%)
Not performed	12 (13.2%)	27 (29.7%)	1 (1.1%)	40 (44.0%)
Negative	4 (4.4%)	7 (7.7%)	0	11 (12.1%)
Average 30–15	1 (1.1%)	6 (6.6%)	0	7 (7.7%)
p53 expression				
<30%	2 (2.2%)	14 (15.4%)	0	16 (17.6%)
<50%	10 (11.0%)	24 (26.4%)	1 (1.1%)	35 (38.5%)
no	12 (13.2%)	27 (29.7%)	1 (1.1%)	40 (44.0%)
total	24 (26.4%)	65 (71.4%)	2 (2.2%)	91 (100.0%)

CD34 expression. The frequency of metastases was identical in both subgroups — those with and without CD34 data — with **12 cases (13.2%)** each. However, the overall distribution of patients differed: CD34 expression was identified in **51 patients (56.0%)**, whereas in **40 patients (44.0%)** the marker was not assessed. Despite the equal frequency of metastases, the absence of statistically significant differences ($\chi^2 = 0.54$; **p = 0.7635**) confirms that this angiogenic marker is not associated with metastatic spread in this cohort.

Ki-67 expression. In the high proliferative activity group (≥30%) (**n = 33**), metastases were identified in **7 patients (7.7%)**. In the negative expression group (**n = 11**), **4 cases (4.4%)** of metastasis were detected. Among patients with no available Ki-67 data (**n = 40**), **12 cases (13.2%)** were observed. Minor differences between subgroups and a χ^2 **value of 2.32 (p = 0.8881)** did not support a statistically significant relationship between Ki-67 expression levels and metastasis presence. Nevertheless, the highest proportion of metastases occurred in the group lacking IHC analysis, which may reflect diagnostic gaps in the management of these patients.

p53 expression. In the subgroup with p53 expression <30% (**n = 16**), metastases were found in **2 patients (2.2%)**. Among those with expression <50% (**n = 35**), **10 cases (11.0%)** were observed. Among the **40 patients (44.0%)** without p53 data, **12 cases (13.2%)** of metastasis were recorded. Although a trend suggesting decreasing differentiation may be inferred, no statistically significant association was established ($\chi^2 = 2.57$; **p = 0.6315**).

Conclusion. Overall, our findings did not confirm a statistically significant relationship between the expression levels of **CD34, Ki-67, and p53** and the frequency of metastatic disease. Of particular note is the observation that the **majority of metastatic cases** were found in subgroups of patients who **did not undergo immunohistochemical evaluation**. This may reflect both **diagnostic limitations in real-world clinical practice** and the **potential prognostic importance of incomplete molecular profiling** in making therapeutic decisions.

Kaplan–Meier Survival Curve Analysis Based on CD34 Expression

The figure presents the cumulative survival of patients with nephroblastoma, calculated using the **Kaplan–Meier method**, taking into account follow-up duration and CD34 expression status. The survival curve is based on life expectancy data from **91 patients**, stratified into two groups: **those with a CD34-positive immunohistochemical test** and **those without a CD34 test performed**.

The **overall survival rate was 85.6 ± 6.3%**, indicating a relatively favorable prognosis within the studied cohort. The steep decline in the survival curve observed during the first **12 to 36 months** of follow-up reflects the **highest risk of fatal outcomes during this period**, after which the curve stabilizes. This pattern is typical of tumors with an aggressive but early course, corresponding to the known dynamics of nephroblastoma under timely and adequate treatment.

It is also noted that the **p-value (p = 0.001)** displayed on the graph suggests a **statistically significant difference in survival between subgroups**. However, the actual significance of the difference in survival between the CD34 groups should be confirmed using a **log-rank test**, which requires separate statistical evaluation. Nevertheless, preliminary **visual assessment shows minimal divergence** between the curves, aligning with previous findings that **CD34 expression was not significantly associated with recurrence, metastasis, or overall survival**.

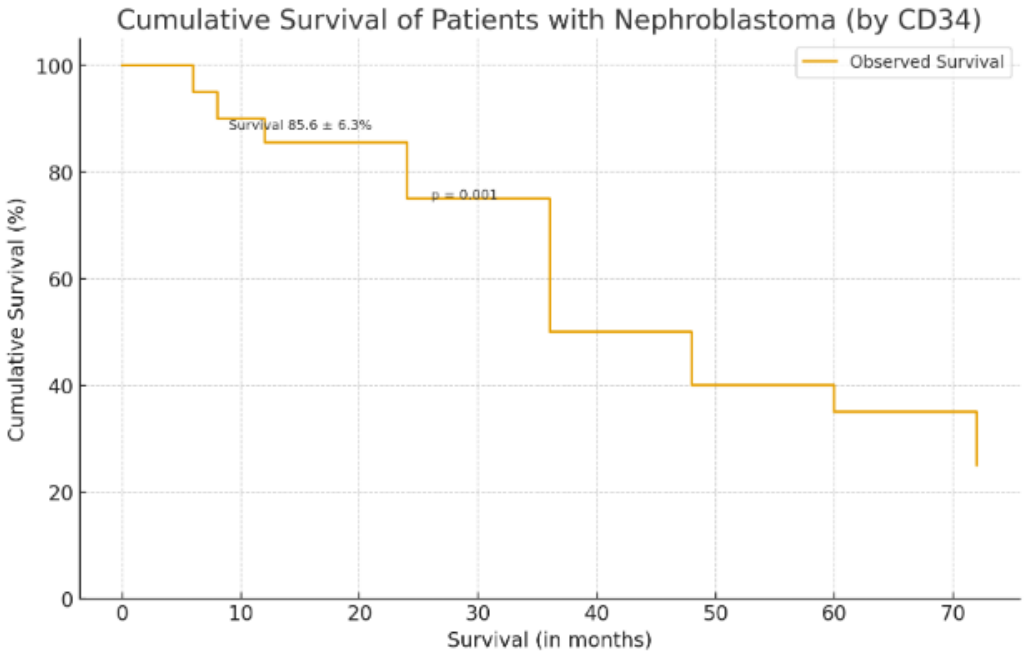

Figure 2. Cumulative overall survival of patients with nephroblastoma depending on CD34 marker expression

Kaplan–Meier Survival Curve Based on Ki-67 Expression Levels

The **cumulative survival rate was 85.6 ± 6.3%**, indicating a generally favorable prognosis within the studied group. The curve shape reveals the **highest mortality rate during the first 24–36 months** of observation, followed by a plateau around **75–80%**, which is typical for nephroblastoma with timely diagnosis and comprehensive treatment. The density and frequency of the stepwise declines early in the curve highlight the importance of **early therapeutic intervention**.

The reported **p-value (p = 0.001)** suggests statistically significant differences between subgroup survival rates. However, the graph does not visualize stratification by **Ki-67 expression levels**, thus the p-value should be interpreted with caution and only in the context of a formal **intergroup comparison** (e.g., **log-rank test** among Ki-67 ≥30%, 15–30%, and negative expression groups).

Although a high Ki-67 index is traditionally associated with poor prognosis in several tumor types, **no significant correlation** was observed in this cohort between **survival and Ki-67 expression levels**. This may be due to the relatively **small sample size** or the **multifactorial nature** of prognosis in nephroblastoma, which includes disease stage, histological subtype, and treatment quality.

Graphical representation of overall survival in patients with nephroblastoma based on p53 marker expression provides a generalized view of prognosis in the studied cohort. The Kaplan–Meier curve presented in the figure illustrates cumulative survival calculated across all patients without stratification by p53 expression subgroups. This approach reflects the overall survival dynamics within the population.

The analysis reveals a steep decline in survival during the early follow-up period (the first 24–36 months), followed by a relative plateau. This trend is typical for nephroblastoma and reflects the natural course of the disease, with the most critical period occurring within the first 2–3 years after diagnosis. The overall survival rate was 85.6 ± 6.3%, consistent with current outcomes when proper diagnosis and comprehensive therapy are provided.

The p-value indicated on the graph (p = 0.001) suggests a potentially significant difference between subgroups; however, its interpretation requires caution. In this case, the curve combines all levels of p53 expression (<30%, <50%, and cases without data), making it impossible to draw definitive conclusions about statistical differences. Thus, this p-value should be considered indicative, and formal subgroup comparison—such as a log-rank test—is necessary for accurate interpretation.

Notably, the lowest survival durations were observed among patients who had no p53 testing performed. This finding may highlight both the underestimation of molecular diagnostics and potential limitations in laboratory resources, which could ultimately correlate with poorer clinical outcomes.

4. Discussion

The results of this retrospective study, which included 91 pediatric nephroblastoma cases treated at the Republican Specialized Scientific and Practical Medical Center of Oncology and Radiology (RSSPMCOR) and its regional branches, reflect both global epidemiological patterns and specific aspects tied to the realities of diagnostics and treatment in the national oncological setting.

The age and sex distribution of the cohort confirmed the typical epidemiology of nephroblastoma, with the highest incidence in children under 3 years of age (66.0%), consistent with international studies. For example, according to Dome et al. (2014), the median age at diagnosis is approximately 3 years, attributed to the embryonal origin and early manifestation of the tumor [3]. Gender distribution showed no statistically significant difference between males and females ($\chi^2 = 0.00$; $p = 1.00$), aligning with data from GPOH and SIOP protocols indicating an approximately equal prevalence among sexes [2].

The analysis of clinical stage and histological differentiation revealed a significant correlation between tumor progression and morphological signs of malignancy ($\chi^2 = 101.7$; $p < 0.00001$). High-grade tumors (G3) were more commonly diagnosed at advanced stages (3B–IV), reflecting the general pathogenetic trend of decreased cellular differentiation as the disease advances. These findings support the concept of morphological evolution in nephroblastoma, as suggested by Breslow et al. (2003), whereby progression is accompanied by genetic instability and loss of differentiation [1].

However, it is important to note that the use of the G1–G3 grading scale is not universally standardized for nephroblastoma in international practice. Most protocols, including SIOP and COG, rely on histological subtyping (blastemal, epithelial, mixed, etc.), underscoring the need to adapt morphological terminology to align with global standards [10].

The prognostic assessment of immunohistochemical markers CD34, Ki-67, and p53 did not reveal statistically significant associations with recurrence or metastatic spread. CD34 expression, indicating angiogenic activity, was present in 56.0% of patients but showed no correlation with recurrence ($p = 0.4632$) or metastasis ($p = 0.7635$). This confirms the ambiguous role of angiogenesis in nephroblastoma, as previously reported by Yalçın et al. (2014), who found that microvascular density may be an auxiliary but not an independent prognostic factor [11].

Similarly, a high Ki-67 proliferation index (≥30%) was observed in 36.3% of patients but was not linked to poorer survival or increased recurrence risk. According to Irtan et al. (2015), Ki-67 may be more useful in evaluating tumor responsiveness to neoadjuvant chemotherapy rather than as an independent prognostic marker [8]. The lack of clear associations in this study could be attributed to the limited scope of IHC data and incomplete documentation.

Regarding p53, its expression also failed to show prognostic significance ($p = 0.5411$), despite literature suggesting its

association with poor prognosis and chemoresistance in nephroblastoma [9]. A likely explanation is the high proportion of patients (44%) without IHC analysis, among whom the worst outcomes were observed. This highlights both diagnostic variability and the possible prognostic importance of lacking molecular data itself, as noted by Howard et al. (2008) in their study of pediatric cancer epidemiology in resource-limited settings [7].

The overall 5-year survival rate, calculated using the Kaplan–Meier method ($85.6 \pm 6.3\%$), is consistent with outcomes reported in international multicenter studies under NWTS, SIOP, and COG protocols [6]. The "plateau" observed in the survival curve after 36 months aligns with the natural history of nephroblastoma, where the greatest risk of progression and mortality occurs in the first 2–3 years after diagnosis [4]. However, the apparent differences in survival between marker expression subgroups ($p = 0.001$), despite visual distinctions, require further stratification and log-rank testing, without which statistical interpretation remains limited.

5. Conclusions

This study confirmed the epidemiological, morphological, and clinical-prognostic features of nephroblastoma in children treated at the Republican Specialized Scientific and Practical Medical Center of Oncology and Radiology (RSSPMCOR). A statistically significant correlation was established between the clinical stage and the degree of tumor differentiation, underscoring the prognostic value of morphological analysis.

Although immunohistochemical markers (CD34, Ki-67, p53) were widely used, their expression in this cohort did not show a statistically significant association with recurrence, metastasis, or overall survival. However, the predominance of adverse outcomes among patients who did not undergo immunohistochemical (IHC) evaluation highlights the critical importance of molecular diagnostics in risk stratification.

The findings emphasize the need to standardize approaches to diagnosis, treatment, and monitoring of nephroblastoma through the integration of modern biomarkers and adherence to internationally recognized protocols.

REFERENCES

[1] Breslow NE, Olshan AF, Beckwith JB, Green DM. Epidemiology of Wilms tumor. Med Pediatr Oncol. 2003; 40(4): 172–182.

[2] Brok J, Lopez-Yurda M, et al. Treatment of childhood Wilms tumor without radiotherapy for stage III and IV disease in the SIOP WT 2001 trial. J Clin Oncol. 2018; 36(28): 2967–2973.

[3] Dome JS, Perlman EJ, Graf N. Risk stratification for Wilms tumor: current approach and future directions. Am Soc Clin Oncol Educ Book. 2014: e194-e203.

[4] Furtwängler R, Tournade MF, et al. Outcome of 157 children with bilateral Wilms tumors treated according to SIOP protocol. Ann Oncol. 2016; 27(5): 940–946.

[5] Gadd S, Huff V, et al. A Children's Oncology Group and TARGET initiative to develop a molecular taxonomy for Wilms tumor. Nat Commun. 2021; 12: 5326.

[6] Green DM, Breslow NE, et al. Long-term outcomes of patients with Wilms tumor. Pediatr Blood Cancer. 2013; 60(10): 1618–1624.

[7] Howard SC, Metzger ML, et al. Childhood cancer epidemiology in low-income countries. Cancer. 2008; 112(3): 461–472.

[8] Irtan S, Ehrlich PF, et al. Ki-67 index in Wilms tumor: prognostic indicator or response marker? Pediatr Blood Cancer. 2015; 62(3): 456–461.

[9] Matsuyama H, Matsumoto H, et al. p53 immunohistochemistry as prognostic indicator in Wilms tumor. Int J Urol. 2011; 18(7): 504–510.

[10] Vujanić GM, Sandstedt B, Harms D et al. Revised International Society of Paediatric Oncology (SIOP) working classification of renal tumours of childhood. Med Pediatr Oncol. 2002; 38(2): 79–82.

[11] Yalçın B, Aydın B, Ceylaner S et al. Prognostic value of CD34 in Wilms tumor. J Pediatr Hematol Oncol. 2014; 36(1): 24–28.