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Original Article

# Distribution of Wilms' Tumor according to age, gender, SIOP clinical staging and various histopathological patterns in a tertiary care hospital Karachi

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**Abstract:**
Background:Wilms' tumor (WT), or nephroblastoma, is the most common malignant renal tumor in children, accounting for 6.7% of pediatric cancers universal.
Objective: To analyze the WT according to age, gender, SIOP clinical staging and various histopathological patterns at Jinnah Postgraduate Medical Centre, Karachi, over a six-year period
Materials and Method: A retrospective analysis of 54 confirmed WT cases was conducted from June 2016 to June 2022. Histopathological and clinical data were obtained, with clinical staging following the SIOP system. Statistical analysis was performed using SPSS version 22, with a significance level set at $p < 0.05$.
Results: Wilms' tumor accounted 3.7% of all pediatric malignancies during the study period. The majority of cases (77.8%) were diagnosed in children less than five years of age, with a mean age of 3.1 years. Males were more frequently affected (57.4%) than females (42.6%), with a male-to-female ratio of 1.35:1. Most tumors were diagnosed at early stages i-e Stage I (46.3%) and Stage II (20.4%). Favorable histology was found in 96.3% of cases, with biphasic (38.88%) and monophasic (22.22%) patterns being the most common.
Conclusion: The study confirms that Wilms' tumor in Pakistan exhibits age and gender distributions similar to global patterns, with most cases presenting at early stages and having favorable histology. Early detection and treatment are essential for better outcomes. Further research into genetic and environmental influences in this population is recommended to improve WT management.

**Keywords:** Childhood malignancies, Histopathology, Nephroblastoma, SIOP staging, Wilms' tumor (WT)

## Introduction:

Wilms' tumor (WT) or Nephroblastoma is the primary malignant kidney tumor of embryonic origin (1). It is the most common childhood renal tumor, second most common intra-abdominal and fifth most common malignant tumor overall (2, 3). It represents about 6·7 percent of overall childhood cancer with an incidence rate of 10 in one million children below the age of 15years annually (4). More than 80% of diagnosed patient's breathe age of less than five years with a mean age of 3.5years (5).

The incidence, behavior and outcome of Wilms' tumor may vary according to the geographical location and ethnicity. Comparatively black African-American children have high incidence of Wilms' tumor than the whites (6). In United States annually diagnosed patients are nearly 500 in number (7). In India reported 11% contribution of Wilms' tumor among all childhood malignancies (8). The collective cancer registry report of Shaukat Khanum

Cancer hospital Pakistan (I994-2023) reported more than 500 cases of Nephroblastoma, contributing 4.8 percent of top 10 malignancies seen in children less than 18years of age of both sexes (9).

Wilms' tumor is mostly sporadic while 01-02 percent of cases are familial. Among unilateral disease male to female ratio is 0.92 and in bilateral it is 0.6.At presentation the median age in unilateral disease is 44 months, 32 months in bilateral disease, while 36.5 months in male and 42.5 months in females respectively. Occasional examples of Wilms' tumor have been described in adults. In adults it is often in distinguishable in its clinical presentation from other more common renal tumors (10).

Histological characteristics play an important role as most powerful prognostic indicator for WT. Histological classic WT is Triphasic composed of blastemal, stromal and epithelial cells in variable proportions. Apart from Triphasic, monophasic and biphasic patterns are also commonly seen. Presence of extra renal tissues like bone, cartilage and muscles make it a Teratoid tumor. Biological behavior of monophasic pattern is shown to be highly aggressive (11). If tumor is diagnosed early with predominantly epithelial pattern shows low aggressiveness and are commonly classified at Stage-I. However, if diagnosed at advanced stage tumor tends to be non- responsive to therapy. Tumors with predominantly blastemal pattern are highly aggressive but considered good responder to chemotherapy (12).

On the basis of histopathology WT can be classified in two prognostic groups. Favorable histology which includes tumor that mimics histological development of normal kidney consisting of epithelial, blastemal and stromal components. While un-favorable histology which includes tumor that's histology characterized by Anaplasia. The aim of this study is to analyze the age and gender distribution of WT cases at Jinnah Postgraduate Medical Centre (JPMC), Karachi, Pakistan, over a six-year period.

**Methodology:**

This study was conducted in collaboration between BMSI, JPMC and National Institute of Child Health (NICH) at the department of Pathology. A total of 54 diagnosed cases of Wilms' tumor by renal biopsies and nephrectomy specimens which were received in the department of pathology NICH from June 2016 to June 2022 were analyzed. Clinical staging was done according to SIOP staging system. All properly formalin fixed paraffin-embedded surgical pathology specimens of renal tumors received at the department of Pathology, NICH, during the previously mentioned time period. Poorly fixed tissue, renal tumors other than Wilms' tumor and metastatic renal tumors were excluded.

The data feeding and analysis was done on computer package SPSS (Statistical Packages of Social Sciences) version 22. In all statistical analysis only P value <0.05 was considered significant.

**Results:**

**Table 1: Incidence of Wilms' tumor (n=54)**

| Years | Total number of Malignancy in all sites | Wilms' tumor | Percentage |
|---|---|---|---|
| 2016 | 36 | 01 | 3.7% |
| 2017 | 83 | 02 | |
| 2018 | 101 | 04 | |
| 2019 | 235 | 12 | |
| 2020 | 433 | 21 | |
| 2021 | 435 | 11 | |
| 2022 | 133 | 03 | |
| **Total** | **1456** | **54** | |

Table1: shows the frequency of Wilms' tumor. The seven years' data shows that total malignancies from all sites were 1456 and out of those 54 cases of Wilms' tumor were found. Frequency of Wilms' tumor was 3.7% over a seven-year period.

**Table 2: Distribution of Wilms' tumor among different age group (n=54)**

| Age | Frequency | Percentage |
|---|---|---|
| < 5 years | 42 | 77.8 |
| 6-10 years | 11 | 20.4 |
| 10-15 years | 01 | 01.8 |
| >15 years | 00 | 00 |

| | | |
|---|---|---|
| **Total** | **54** | **100** |

Table 2: shows the age distribution of Wilms' tumor. The age range was 0-15 years of age with majority of the patients 42/54 (77.8%) belonging to the age group <*5* years of age followed by11 (20.4%) age range group 6-10 years of age. Only 01 patient (1.8%) was found at age of 11-15 years and no patient with this lesion is seen in more than I*5* years of age group. Mean age was 3.1 years.

**Figure 1: Gender wise distribution among cases of Wilms' tumor (n=54)**

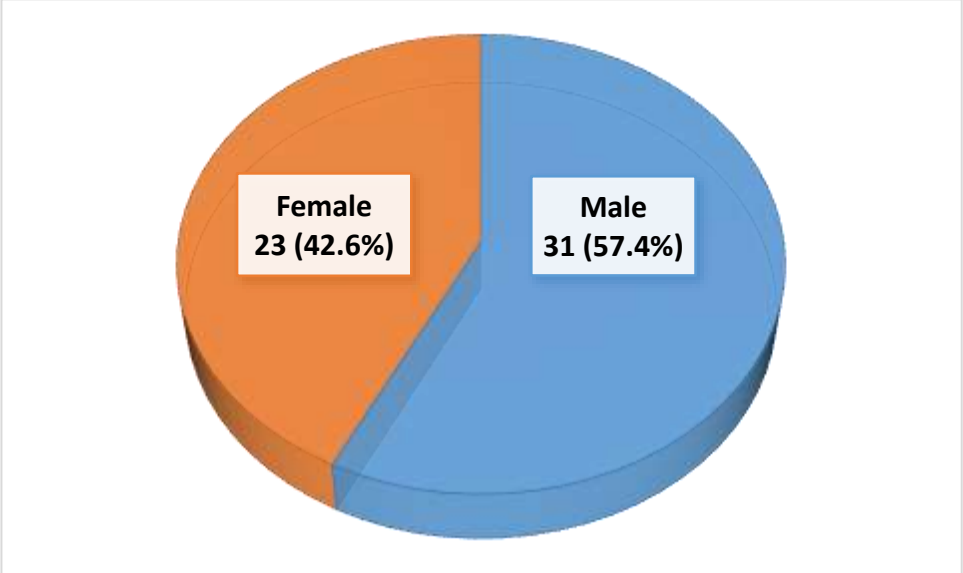


Figure 1: shows the distribution of Wilms' tumor according to the gender. Most of the cases 3I (57.4%) seen were males and 23(42.6%) were females. Mean age in females was 3.5 whereas it was 03 in males. The male to female ratio was1.35:1.

**Figure 2: Distribution of Wilms' tumor according to SIOP clinical staging system**

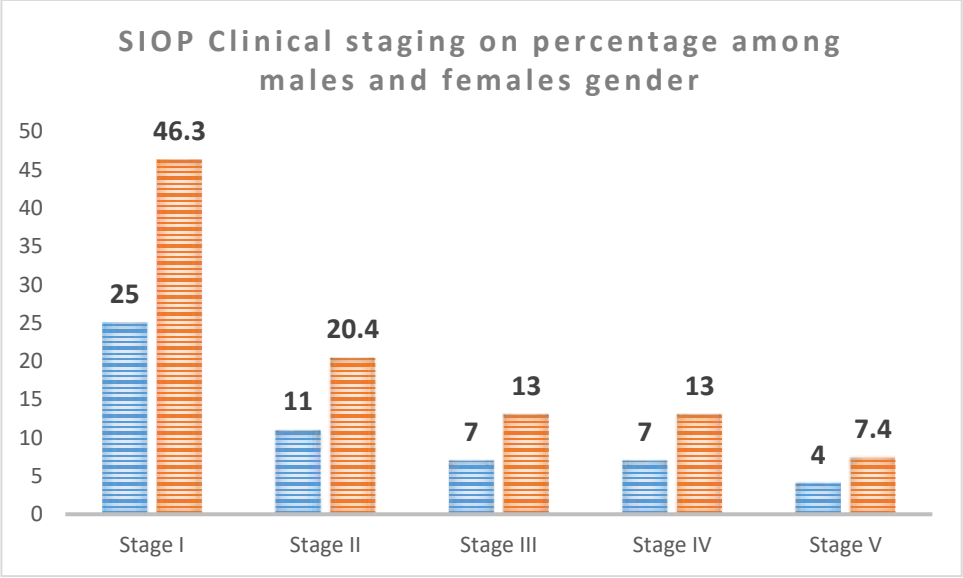


Figure 2: shows distribution of Wilms' tumor according to the SIOP clinical staging system. Out of 54 cases majority were found in stage 1 (n=25, 46.3%) and stage II (n=11, 20.4 %).This is followed by stage III (n=07, 13%) and IV showed 07 cases (n=07, 13%) each. Stage V showed 04 cases (7.4 %) which was the least percentage among all.

**Table 3: Distribution of Wilms' tumor according to different histopathological pattern (n=54)**

| Histopathological Grade | | Number of cases | | Percentage | |
|---|---|---|---|---|---|
| Favorable histology | Monophasic | 12 | 52 | 22.22% | 96.29 |
| | Biphasic | 21 | | 38.88% | |
| | Triphasic | 11 | | 20.37% | |
| | Teratoid | 08 | | 14.81% | |
| Un-favorable histology | | 02 | | 3.7% | |
| **Total** | | **54** | | **100%** | |

Table 3: shows distribution of Wilms' tumor according to different histopathological grade. Out of 54 cases of Wilms' tumor majority were found in favorable histology i.e. 52 cases (96.3%) including most of the cases in [biphasic pattern i-e (38.88%) followed by monophasic pattern (22.22%), Triphasic pattern (20.37%) and Teratoid pattern (I4.81%)]. The un-favorable pattern was seen in 02 /54 (3.7%) cases.

**Table 4: Association of SIOP clinical stage and histopathological pattern of Wilms' tumor (n=54)**

| Histopathological Grade | | Stage I | Stage II | Stage III | Stage IV | Stage V | Total | P value |
|---|---|---|---|---|---|---|---|---|
| Favorable Histology | Monophasic | 02 | 02 | 03 | 02 | 03 | 12 | 0.002 |
| | Biphasic | 07 | 07 | 04 | 03 | 00 | 21 | |
| | Triphasic | 11 | 00 | 00 | 00 | 00 | 11 | |
| | Teratoid | 05 | 02 | 00 | 01 | 00 | 08 | |
| Un-favorable histology | | 00 | 00 | 00 | 01 | 0l | 02 | |
| **Total** | | **25** | **11** | **07** | **07** | **04** | **54** | |

Table 4 shows the association of SIOP clinical stage with the histopathological grade of Wilms' tumor. Out of 54 cases 52 were with favorable histology including 12 (22.22%) with monophasic 21(38.88%), biphasic 11 (20.37%) Triphasic and 08(14.81%) Teratoid pattern. Out of 12 monophasic 02 (3.7%) were stage I, 02 (3.7%) stage II, 03 (5.55%) stage III, 02 (3.7%) stage IV and 03 (5.55%) stage V. Out of 21 biphasic 07 (12.96%) were stage I and II each, 04 (7.40%) stage III and 03 (5.55%) stage IV. All of the Triphasic (20.37%) were stage I. Out of 08 Teratoid 05 (09.30%) were stage I, 02 (3.7%) stage II and l (l.8%) stage IV. 02 out of 54 cases of Wilms' tumor was with un-favorable histology 01 (1.8%) of which was stage IV and 01(1.8%) was stage V. P value is 0.002.

**Discussion**:

Wilms' tumor is the most common pediatric renal tumor and accounts for 95% of all malignant neoplasm's of the kidney in children. In the present study we attempted to determine the frequency, gender wise distribution, histopathological pattern and according to SIOP clinical staging system of Wilms' tumor.

Frequency of Wilms' tumor in the present study was found to be 3.7 %. This was in close conformity with the data reported by Shaukat Khanum cancer registry (Cancer statistics, 2023) that showed 4.8% (9). The data published by Agrawal et al, (2022) and Sathish et al, (2022) showed 4.7% contribution of Wilms' tumor amongst childhood malignancies (8, 13). Pakistan being a developing country there is no population based tumor registry in Pakistan; therefore, the exact incidence of different cancers in Pakistan remains unknown.

In the present study the mean age of the patient with Wilms' tumor was calculated to be 3.1 years. Similar findings were observed by Ikhuoriah et al, (2023), Nasir et al, (2024), and Ghafoor et al, (2020) showed 3.5 years (3, 14, 15). In the present study the median age for male was 03 years and 3.5 years for females. This finding was in total agreement with the work by Bhutani et al, (2021) reported median age for males and females 2.6 years and 2.8 years respectively (16)

The most commonly affected age group in our study was less than 05 years of age in (77.8%) cases. Our findings are comparable to the figures documented in the study by Ghafoor et al, (2020) reported 80% of cases and Nasir et al, (2024) who observed 75% cases for <5 years of age (14,15). A notable finding in the present study was that a single patient at 11years of age was found with this lesion. Rehman et al, (2021) also reported a single case of Wilms' tumor in same age group (17). One of the reasons for this could be that the exact age of the patient was not known by the parents as most of the patients reporting to NICH are from uneducated background.

Regarding gender distribution of the Wilms' tumor in our study there was a slight male predominance (male to female ratio1.35:1) which is similar to the studies by Bhutani et al, (2021), Nasir et al, (2024), Bushra et al, (2024) (15, 16, 18). But, this is dissimilar to the study by Abdul Wahab et al, (2022) that shows female

predominance (19). The male predominance in our study could be due to gender bias in our culture where males are brought preferentially to medical attention than females.

According to the SJOP staging system most of our cases i.e.79.7% was found in stage I, II and III, whereas 20.4% cases were in stage IV and V. Our findings closely correspond with Zabolined et al, (2006) reporting 79% of cases in stage I, II and III while 20.9% in stage IV and V (20). Kidney tumor (Ekenze et al, 2006) have also been reported in majority of the cases in stages I, II and Ill (74.5%) followed by stage IV and V i.e. 25.5 %.(21)

In the present study majority of the cases were found with favorable histologyi.e. 96.3%. A study by Das et al, (2012) observed 94.4% Jadali et a,l (2011) reported 75% and Seyed-Ahadi et al, (2007) found54.4% cases with favorable histology (22–24). A study by Das et al, (2012) showed 5.6%cases with un-favorable histology (22).Sternberg's diagnostic surgical pathology also quoted 05%cases with un-favorable histology. On the contrary Jadali et al, (2011) found 25% cases and Seyed-Ahadi et al, (2007) revealed 43.6%cases with un-favorable histology. The variation could be due to environmental, dietary and genetic difference (23, 24).

In the present study we found significant correlation (p-value 0.002) between the histopathological grade and the clinical stage of the tumor. Whereas, Das et al, (2012) observed no correlation between histopathological grade and clinical stage of the tumor (22).The reason for this discrepancy may be due to the large sample size included in the present study.

Among favorable histology in this series 46.29% cases were in stage I, 20.37% in stage II, 12.96% stage III 11.11%stage IV and5.5% stage Zabolined et al, also showed majority of the cases with favorable histology in stage I, II, and III(20). In our series none of the cases of un-favorable histology was seen in stage I, II and III as all were seen in stag IV and V. These results are well in line with the other studies.(18, 19)

**Conclusion:**

This study demonstrates that Wilms' tumor in Karachi primarily affects children under five years, with a slight male predominance. Most cases are diagnosed at early stages and exhibit favorable histology, which is crucial for better treatment outcomes. The findings emphasize the need for early detection and proper staging to improve prognosis. Further research into genetic and environmental factors influencing Wilms' tumor in this population is recommended.

**Author's contribution**

**ZS, IMS, GS** → conceived/design, analysis and editing of manuscript

**KSM, MA, AH & PJA** → helps in data collection, drafting the work, manuscript and statistical analysis

**ZS, IMS & GS** → did review final approval of manuscript and agreement to be accountable

**Conflict of interest;** the authors declare non-financial competing interests

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