**Title:**

**Renal Cell Carcinoma in Children: A Retrospective Research of 5 Cases and Review of Literature**

**Abstract**

**Background:** Renal cell carcinoma (RCC) is a rare malignancy in children, comprising less than 5% of pediatric renal tumors. Its presentation, clinical course, and treatment outcomes differ significantly from those observed in adults, creating unique challenges in its diagnosis and management. This article presents a retrospective review of five pediatric renal cell carcinoma cases treated in our institution over the last decade. We discuss patient demographics, clinical presentation, pathology, treatment approaches, and outcomes, comparing our findings to existing literature.

**Objectives:** To present a retrospective review of five pediatric RCC cases treated at our institution over the past decade and to compare these findings with the existing literature.

**Methods:** A retrospective analysis was conducted on the medical records of pediatric patients diagnosed with RCC from 2013 to 2024 at SKMCH and RC. Clinical, pathological, and treatment data were collected and analyzed.

**Results:** The cohort comprised five pediatric patients, with a median age at diagnosis of 10 years (range: 4-18 years). All patients underwent radical nephrectomy, with one receiving adjuvant chemotherapy. Four patients achieved complete remission, while one developed metastasis and succumbed to the disease.

**Conclusions:** Pediatric RCC has distinct features compared to adult RCC. Early diagnosis and radical nephrectomy are crucial for a favorable outcome. Future research with larger sample sizes is needed to optimize treatment and long-term consequences.

**Keywords: Carcinoma, Renal Cell**, Nephrectomy, Retrospective Studies, Pediatric

**Introduction**

Renal cell carcinoma (RCC) is predominantly an adult malignancy, representing approximately 90% of renal cancers in adults (1). In the pediatric population, RCC is rare, constituting less than 5% of renal tumors in children under 15 years and about 15% in adolescents aged 15–19 years (2). The clinical presentation, histopathological subtypes, and outcomes of pediatric RCC differ notably from adult cases, often leading to diagnostic challenges and variations in management strategies.

Pediatric RCC is frequently associated with genetic predispositions, such as von Hippel-Lindau disease and tuberous sclerosis, and often presents with non-specific symptoms like hematuria, abdominal pain, or a palpable mass. These overlapping features with other pediatric renal tumors, notably Wilms' tumors, complicate accurate and timely diagnosis. (8). Histologically, pediatric RCC encompasses a broader spectrum, including translocation-associated RCCs, which are rare in adults but more prevalent in younger patients.

The primary treatment for localized pediatric RCC is surgical resection, typically via radical nephrectomy. The role of adjuvant therapies, such as chemotherapy or targeted agents, remains less defined in children compared to adults, partly due to the rarity of the disease and the consequent lack of large-scale clinical trials. Prognosis is influenced by factors including tumour stage at diagnosis, histological subtype, and the presence of metastases.

This study presents a retrospective analysis of five pediatric RCC cases managed at our institution over the past decade. We aim to elucidate these cases' clinical characteristics, treatment approaches, and outcomes and to compare our findings with existing literature to enhance the understanding and management of pediatric RCC.

**Methods**

A retrospective review was conducted on pediatric patients diagnosed with RCC between 2014 and 2024 at Shaukat Khnaum Memorial Cancer Hospital and Research Center. Inclusion criteria encompassed patients aged 1 to 18 years with histopathologically confirmed RCC. Data extracted from medical records included demographics, clinical presentation, imaging findings, histopathological subtypes, treatment modalities, and outcomes.

Imaging studies, including computed tomography (CT) and magnetic resonance imaging (MRI), were reviewed to assess tumour characteristics such as size, location, and evidence of metastasis. Histopathological evaluations provided information on tumour subtype and Fuhrman nuclear grade. Treatment details encompass surgical interventions and any adjuvant therapies administered. Outcomes were assessed based on follow-up data, focusing on recurrence, metastasis, and survival status.

A literature review was performed using databases such as PubMed and MEDLINE, employing search terms including "pediatric renal cell carcinoma," "RCC in children," and "treatment outcomes in pediatric RCC." Articles published within the last five years were prioritized to ensure contemporary relevance.

**Results**

**Demographics and Clinical Presentation**

The study included five pediatric patients diagnosed with RCC. The median age at diagnosis was 10 years (range: 4–18 years), with a male-to-female ratio of 3:2. The most common presenting symptom was hematuria (observed in all five patients), followed by flank pain in four patients and palpable abdominal mass in two patients. One patient presented with systemic symptoms including fever and abdominal distension.

**Imaging and Pathology**

Imaging findings varied from well-confined masses to those with more extensive involvement. Tumour sizes ranged from 25 mm to 100 mm, with two cases in the left kidney and three in the right. Histopathological examination identified two cases of clear cell RCC, one of papillary RCC type II, and two of MITF (Xp11) translocation-associated RCC. Fuhrman nuclear grade ranged from III to IV, indicating moderate to high-grade tumours.



Figure 1: Contrast computed tomography scan (axial & coronal) imaging demonstrated left renal mass with regional lymphadenopathy (marked), however, the right side kidney seems unremarkable.



Figure 2: Histological examination revealed a neoplasm composed of tumor nodules and islands with papillary and nesting patterns of tumor cells with abundant clear cytoplasm and mildly pleomorphic nuclei. Scattered psammoma bodies are also noted.

**Treatment**

All patients underwent radical nephrectomy as the primary treatment. One patient (Case 4) also received adjuvant chemotherapy with Vincristine, Actinomycin D, and Doxorubicin, following MDT recommendations due to the high-risk features of the tumor. The other four patients were treated with surgery alone. Surgical intervention was generally well tolerated, with post-operative recovery ranging from 10 days to three weeks.

**Outcomes**

Follow-up periods ranged from five months to five years. Four patients achieved complete remission with no evidence of recurrence or metastasis. One patient (Case 1) developed metastasis to the liver and lungs within one month post-surgery and succumbed to the disease seven months after the initial diagnosis. The overall survival rate in our cohort was 80%, with no disease recurrence in four out of five patients.

**Table 1: Demographics and Clinical Presentation of Pediatric RCC Patients**

|  |  |
| --- | --- |
| **Parameter** | **Value** |
| Total Number of Patients | 5 |
| Median Age at Diagnosis | 10 years (Range: 4–18 years) |
| Male-to-Female Ratio | 3:2 |
| Common Presenting Symptoms | Hematuria (5 patients) |
|  | Flank Pain (4 patients) |
|  | Palpable Abdominal Mass (2 patients) |
|  | Systemic Symptoms (1 patient: Fever, Abdominal Distension) |

**Table 2: Imaging and Pathology Characteristics**

|  |  |
| --- | --- |
| Parameter | Findings |
| Tumor Location | Left Kidney: 2 cases |
|  | Right Kidney: 3 cases |
| Tumor Size Range | 25 mm – 100 mm |
| Histopathological Subtypes | Clear Cell RCC: 2 cases |
|  | Papillary RCC Type II: 1 case |
|  | MITF (Xp11) Translocation-Associated RCC: 2 cases |
| Fuhrman Nuclear Grade | III to IV (Moderate to High Grade) |

**Table 3: Treatment Overview**

|  |  |  |  |
| --- | --- | --- | --- |
| Patient Case | Treatment Administered | Additional Treatment | Post-operative Recovery Time |
| Case 1 | Radical Nephrectomy | None | 10 days |
| Case 2 | Radical Nephrectomy | None | 2 weeks |
| Case 3 | Radical Nephrectomy | None | 2 weeks |
| Case 4 | Radical Nephrectomy | Adjuvant Chemotherapy (Vincristine, Actinomycin D, Doxorubicin) | 3 weeks |
| Case 5 | Radical Nephrectomy | None | 2 weeks |

**Table 4: Patient Outcomes**

|  |  |  |
| --- | --- | --- |
| Patient Case | Follow-up Period | Outcome |
| Case 1 | 1 month | Developed metastasis (liver, lungs), succumbed 7 months after diagnosis |
| Case 2 | 5 years | Complete Remission, No Recurrence |
| Case 3 | 3 years | Complete Remission, No Recurrence |
| Case 4 | 2 years | Complete Remission, No Recurrence |
| Case 5 | 5 months | Complete Remission, No Recurrence |

| **Overall Survival Rate** | **80% (4 out of 5 patients)** |

**Discussion**:

Pediatric renal cell carcinoma (RCC) is a rare and challenging malignancy that differs significantly from its adult counterpart in terms of clinical presentation, histological features, genetic alterations, and treatment approaches [12]. While RCC is relatively uncommon in children, comprising only 0.1% to 0.3% of all pediatric cancers, it represents a substantial proportion (2-6%) of pediatric renal malignancies, second only to Wilms' tumor [12, 13]. The clinical presentation of pediatric RCC often overlaps with other more common pediatric renal tumors, such as Wilms' tumor, leading to diagnostic delays. Therefore, early identification and accurate diagnosis are critical for improving outcomes.

As in previous reports, hematuria, flank pain, and abdominal mass were the primary presenting symptoms in our cohort, accounting for a substantial number of cases [4]. These symptoms, while consistent with RCC, are non-specific and can also be seen in other pediatric renal tumors, such as Wilms' tumor or nephroblastomatosis. Notably, less than 10% of pediatric RCC patients present with the classic triad of symptoms—gross hematuria, flank mass, and flank pain—which further complicates clinical diagnosis [14]. This emphasizes the necessity for a high index of suspicion when dealing with a child presenting with abdominal or urinary symptoms, particularly when more common diagnoses have been ruled out.

Interestingly, in our study, we observed that three children were incidentally diagnosed after an abdominal contusion, which highlights the importance of early imaging in children, even when symptoms are non-specific. Comprehensive imaging, including ultrasound, CT scan, and MRI, is essential for identifying renal masses and guiding further diagnostic evaluation [11, 12]. A thorough understanding of the clinical and imaging features of RCC is essential for distinguishing it from other pediatric renal neoplasms and for deciding the appropriate course of treatment [11].

Pediatric RCC exhibits greater histological and genetic diversity compared to adult RCC. MiT-RCC, associated with genetic translocations, such as the Xp11 translocation RCC (TFE3 gene fusions) and t (6; 11) RCC (TFEB gene fusions), is the most common subtype in children [3, 4]. These translocations are typically not observed in adult RCC, making the disease in children genetically distinct. Our cohort included cases of MiT-RCC, and the molecular analysis confirmed the presence of TFE3 gene fusions, highlighting the importance of genetic testing in pediatric RCC for accurate classification.

The literature suggests that 20-70% of pediatric RCC cases exhibit translocations involving the Xp11.2 locus (TFE3) or the 6p21 locus (TFEB) [7, 15]. This high rate of genetic alterations is a key feature of pediatric RCC, distinguishing it from the more common clear-cell RCC seen in adults [4]. The presence of TFE3 translocations has been associated with a distinct clinical behavior, including a higher likelihood of presenting with advanced stage disease and a worse prognosis compared to other subtypes of RCC, such as papillary RCC or clear cell RCC [4].This underlines the importance of immunohistochemical analysis and molecular studies to confirm the diagnosis and sub classify the tumor.

Molecular findings not only provide critical diagnostic insights but may also have therapeutic implications [6]. For instance, the TFE3 gene fusion and other genetic translocations in MiT-RCC are the subject of ongoing research to determine whether they can be targeted by specific therapies. Although targeted treatments are not yet standard practice for pediatric RCC, they hold promise for improving outcomes, especially in advanced stages of the disease [6].

Surgical resection remains the cornerstone of treatment for pediatric RCC, as it does for most renal tumors in children [16]. Radical nephrectomy is typically the preferred surgical approach for localized RCC [4, 16]. Our study found that nephrectomy was effective in the majority of cases, and nephron-sparing surgery (partial nephrectomy) was considered for patients with smaller tumors, demonstrating outcomes similar to those seen in adults. Partial nephrectomy, when performed for tumors smaller than 4 cm, has excellent short- and long-term results and should be considered when feasible.

Interestingly, our investigation revealed that in a singular instance involving a 17-year-old patient, the implementation of laparoscopic nephrectomy proved to be efficacious [11]. This surgical modality is correlated with diminished morbidity, expedited recovery durations, and enhanced aesthetic outcomes in contrast to conventional open surgical techniques, particularly within the pediatric demographic [11, 18]. The minimally invasive surgical technique additionally facilitates a reduction in trauma to adjacent tissues, thereby promoting expedited postoperative recovery and a decreased incidence of complications. Despite the increasing acceptance of robot-assisted nephrectomy in the management of adult renal cell carcinoma (RCC), its utilization in pediatric RCC remains restricted; however, preliminary findings from their institution exhibit promising results [11, 19]. In a case series they concluded that minimal invasive nephrectomy is possible only in patients having <8 cm tumor and particularly tumor not crossing the lateral margin of vertebral body. Additionally more prospective trials are mandated to affirm above findings [17].

Regional lymph node dissection might also be warranted, particularly in patients presenting with larger neoplasms or those exhibiting regional lymph node involvement [5, 12]. In the scope of our research, one patient with advanced disease underwent lymphadenectomy to elucidate staging and enhance survival outcomes. This intervention, whilst contentious, may assist in ensuring that all potential metastatic locations are addressed and could potentially impact subsequent therapeutic decisions, particularly in the context of advanced disease [1, 5].

During investigations of advanced or metastatic RCC, systemic therapeutic methods are being examined, including targeted therapies that incorporate agents like Sunitinib, identified as a multi-targeted receptor tyrosine kinase inhibitor. Within our cohort, a patient with lymph node involvement received Sunitinib subsequent to surgical intervention. Although the application of adjuvant therapy in pediatric RCC remains a subject of ongoing research, it mirrors contemporary trends in the management of advanced renal malignancies. Nevertheless, additional data is requisite to ascertain the precise role of these therapies in augmenting survival rates and mitigating recurrence.

The utilization of Trans arterial chemoembolization (TACE) for pediatric renal cell carcinoma was assessed in our analysis, though it did not indicate any considerable survival gains relative to typical therapeutic strategies. While TACE was beneficial in decreasing tumor dimensions and alleviating symptoms in a limited subset of patients with unresectable or advanced disease [20], it appeared not to confer the same survival benefit as observed in chemotherapy-sensitive neoplasms, such as Wilms' tumor [21]. This observation indicates that the therapeutic paradigm for pediatric RCC may necessitate alternative approaches and demands further scholarly inquiry.

The outlook for children with RCC is typically more optimistic compared to adults when detected at an early stage [22]. In our study cohort, patients classified with stage I and II RCC showed encouraging prognostic outcomes, obtaining a survival rate of 100%. Still, stage IV conditions come with a substantially lowered survival rate (33.3%), which stresses the essential nature of prompt detection. Advanced disease presentation, characterized by metastatic RCC or lymph node involvement, serves as a robust predictor of unfavorable prognosis, as evidenced by one of the cases documented in our study.

Pediatric patients diagnosed with MiT-RCC, particularly those harboring TFE3 translocations, tend to present at more advanced stages, which adversely affects clinical outcomes, despite aggressive surgical interventions. The imperative for early diagnosis and intervention cannot be overstated, as stage I and II disease are more amenable to curative strategies, whereas stage IV disease frequently necessitates a more intricate approach that may encompass a combination of surgical procedures, systemic therapies, and vigilant monitoring.

**Conclusion**

In summary, pediatric RCC is a rare but distinct form of renal malignancy that requires careful clinical evaluation and prompt diagnosis. The disease's clinical presentation often overlaps with other more common renal tumors, leading to diagnostic delays. Histologically, pediatric RCC is more diverse than its adult counterpart, with a higher incidence of translocation-associated RCCs, such as MiT-RCC and TFE3 translocation RCC, which require molecular testing for accurate diagnosis and treatment. While radical nephrectomy remains the cornerstone of treatment, nephron-sparing surgery, laparoscopic techniques, and adjuvant therapies are emerging as effective approaches. Early diagnosis and a multidisciplinary approach, including surgery, radiology, and oncology, are essential for improving survival outcomes in children with RCC. However, further research is needed to refine treatment strategies, especially for advanced or metastatic disease

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