

## Original Research Article

**Outcome of germ cell tumors in children after surgical management. A longitudinal study**

### **Abstract**

**Aim:** To assess the outcome of germ cell tumors in children after surgical management.

**Study design:** A longitudinal study

**Place and duration:** Pediatric surgery and oncology department of the national institute of child health Karachi from January 2017 to December 2018

**Methodology:** A total of 79 children between the ages of 0 to 12 years were included in the study. Baseline, ultrasound, CT scan, tumor markers, and biopsy for tissue diagnosis were done. After surgical excision, they were followed up for 12 months with tumor markers, ultrasound and CT Scans for any recurrence. We just observed patients with mature teratoma and did surveillance for immature variety. The rest of the subtypes received JEB chemotherapy (carboplatin, etoposide, and bleomycin) as per UK-based chemotherapy protocol according to their disease stage

**Results:** Most common age of presentation was < 1 month old. The antenatal diagnosis was made in 2 (2.5%) children. Sacrococcygeal region 54 (68.3%) was the most commonly involved region followed by gonads in 17 (21.5%) cases. According to histology mature teratoma was present in 32 (40.5%) children. Complete resection was done in 52 (65.8%) children. Recurrence occurred in one child and 3 children expired.

**Conclusion:** The site of primary disease plays a role in the prognosis of pediatric germ cell tumors with the extra gonadal pelvic tumors being the worst regarding resectability.

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It's not the same police In the current study, the general outcome was good in terms of complete excision in most of the patients. Worst outcome noted in yolk sac tumor. There was a minimal recurrence rate.

**Keywords:** yolk sac tumors, germ cell tumor, recurrence, children

### Introduction

The phrase "paediatric germ cell tumor" refers to malignant tumors of germline cells in children and adolescents aged 0 to 18 years <sup>1</sup>. Cancers of the testis, ovary and extragonadal locations such as the sacrococcygeal region and mediastinum can all develop <sup>2</sup>. First, epidemiologic data suggest two different peaks in GCT incidence, one in young children (aged 0–4 years) and the other in puberty <sup>3</sup>. GCTs account for 15% of malignancies diagnosed during adolescence <sup>4</sup>. GCTs account for roughly 3% of malignancies in children aged 0–18, and their incidence rises with the onset of puberty.

The Malignant Germ Cell Tumor International Collaborative (MaGIC) Consortium was formed in recent years by investigators from the Children's Oncology Group (USA) and the Children's Cancer and Leukaemia Group (UK) to improve outcomes for patients with germ cell tumors (GCTs) by generating new insights into aetiologyetiology, prognosis, toxicity reduction, and optimal treatment <sup>5</sup>.

Surgical resection remains the most important aspect of treatment, and accurate surgical staging is required to determine the appropriate risk-based treatment. Surgery alone is the treatment of

choice for all benign tumors (mature and immature teratoma) and select entirely resectable malignant tumors <sup>6</sup>. In infants and children with unresectable or metastatic cancer, modern chemotherapy is exceedingly successful, and these youngsters have a very good survival rate. The use of neoadjuvant chemotherapy preserves important organs, and excision of vital structures is not necessary at the time of initial presentation. <sup>7</sup>. Surgery's purpose is to get rid of as many tumor cells as feasible. Some germ cell tumors in children, such as testicular germ cell tumors and ovarian germ cell tumors, can be treated with surgery alone. Additional therapy following surgery may be required for others <sup>8</sup>. After formal examination and evidence of irresectability, all children with germ cell tumors had surgery, either curative resection or biopsy, in a local trial. There was no major surgical morbidity or mortality in those patients <sup>9</sup>.

The current study is planned to assess the outcome in children having germ cell tumor who were managed surgically.

**Methodology:** A total of 79 children between the ages of 0 to 12 years were included in the study. Permission was taken from the ethical review committee of the institute. Baseline, ultrasound, CT scan, tumor markers, and biopsy for tissue diagnosis were done. After surgical excision, they were followed for 12 months with tumor markers, ultrasound and CT Scans for any recurrence. We just observed patients with mature teratoma and did surveillance for immature variety. The rest of the subtypes received JEB chemotherapy (carboplatin, etoposide, and bleomycin) as per UK-based chemotherapy protocol according to their disease stage. SPSS version 23 was used for data analysis

**Results:** A total of 79 children were included in the study. The most common age of presentation was < 1 month old. The antenatal diagnosis was made in 2 (2.5%) children (As shown in Table

1). Sacrococcygeal region 54 (68.3%) was the most commonly involved region followed by gonads in 17 (21.5%) cases (As shown in Table The surgical approach for the treatment of germ cell tumors is mentioned in Table 3. According to histology mature teratoma was present in 32 (40.5%) children (As shown in Table 4). Complete resection was done in 52 (65.8%) children. Recurrence occurred in one child and 3 children expired (As shown in Table 5).

Like metastasis is seen in SCT types 3 and 4 that are of yolk sac variety. A total of 2 cases were re-explored for the residual disease of retroperitoneal and SCT type 4 variety.

[What's about tumor markers like AFP ?](#)

**Table 1: Demographic characteristics of the study participants (n=79)**

Gender	Number	Percentage
Male	34	43.0
Female	45	57.0
Antenatal diagnosis	2	2.5
<b>Age at presentation</b>		
<1 month	32	40.5
1 month – 1 year	15	18.9
1-5 years	24	30.3
>5 years	8	10.1

**Table 2: Anatomical locations of germ cell tumors**

Location	Number	Percentage
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Sacrococcygeal region	54	68.3
Gonads	17	21.5
Abdomen	6	7.5
Cervical	2	2.5

**Table 3: Surgical approach for the treatment of germ cell tumors**

Location	Surgical approach
SCT (Type I and II)	Sacral
SCT (Type III and IV)	Abdominal/ Sacral
Ovarian tumor	Oophorectomy
Testicular tumor	Orchiectomy
Retroperitoneal	Excision
Cervical	Excision

**Table 4: Histopathologic findings of germ cell tumors**

Histology	Number	Percentage
Mature teratoma	32	40.5
Yolk sac tumor	15	19.0
Mixed variety	12	15.1
Immature teratoma	9	11.3

Dysgerminoma	7	8.8
Embryonal carcinoma	4	5.0

**Table 5: Outcome of the study participants having germ cell tumor**

<b>Outcome</b>	<b>Number (%)</b>	<b>Histology</b>
Cured	52 (65.8)	
On treatment	13 (16.0)	
Left during treatment	9 (11.0)	
Left before treatment	2 (2.5)	
Metastasis	3 (3.7)	Yolk sac
Recurrence	1 (1.2)	Yolk sac
Expired	3 (3.7)	Immature teratoma/Yolk sac

## **Discussion**

In the current study, females (57%) outnumber males. Most the children presented in the first months of life. The sacrococcygeal region (68.3%) was the most commonly involved followed by the gonads (21.5%). In the case of gonadal involvement oophorectomy and orchiectomy were done. Most of the tumors were mature teratoma followed by yolk sac tumors, mixed variety,

inactive teratoma and embryonal carcinoma. Our 65.5% children completed treatment, while 11% left during treatment, 2.5% left before treatment. Metastasis was present in 3.7% of cases. There was a recurrence in one child while the 3 children died during treatment due to illness.

In a comparable survey conducted in Lahore, Pakistan, females outnumbered males. The most prevalent tumor was the yolk sac tumor, which accounted for 90 (43.5 percent), followed by mixed GCT, which accounted for 40 (19.3 percent). Metastasis occurred in 24 patients (11.6%)<sup>10</sup>. Patients in an international study ranged in age from 3 months to 14 years. The incidence of testicular GCTs reduced as people got older, while the incidence of ovarian GCTs increased. There were 95 benign tumors (74.8 percent) and 32 malignant tumors among the 127 individuals (25.2 percent). The most prevalent benign GCT was mature teratoma, while the most common malignant GCT was yolk sac tumour<sup>11</sup>.

A total of 44 patients were enrolled in the Bangkok research. At the time of diagnosis, the Median age was 1.74 years. A total of 28 patients (64%) had an extragonadal tumour. The sacrococcygeal area was the most prevalent initial tumour location, as it did in our analysis. Surgery was performed on 40 patients (91%) and chemotherapy was administered to 27 patients (61%). Thirty-eight patients (86%) were able to attain remission; three patients (7%) relapsed after a median of one year. Eight patients (18%) died, largely as a result of tumour development<sup>12</sup>.

The result of children with malignant germ cell tumors (MGCT) increased to over 90% 5-year survival in Indian research after the use of cisplatin. Chemotherapy and surgical recommendations for both gonadal and extra-gonadal MGCTs have been revised throughout

time as a result of the findings of many multinational co-operative trials to reduce early and late morbidities while also improving survival <sup>13</sup>.

In a Pakistani study, 69 percent of the 105 patients with gonadal germ cell tumors were females, and 41 percent were children under the age of five. Only 6% of tumors were benign, whereas 94 percent were cancerous. On histology, yolk sac tumors accounted for 49%, mixed malignant germ cell tumors for 12%, dysgerminoma for 12%, teratoma for 8%, juvenile granulosa cell tumors for 5%, Sertoli and Leydig cell tumors for 2%, and the remainder were unidentified. Overall, 18% of people died, with 79 percent dying as a result of illness progression and delayed treatment, and 21% dying as a result of infection <sup>14</sup>.

In an Indian study, 35 boys with extracranial GCT were included. There were 28 individuals with testicular GCT, one with retroperitoneal nodal GCT, one with paraspinal GCT, one with mediastinal GCT, and four with sacrococcygeal teratoma. The most prevalent histological subtype was a mixed germ cell tumour. Patients with testicular GCT were diagnosed with stage IV illness in 16 of 28 cases (57.1%). The most prevalent chemotherapy regimen was Peb (Cisplatin, etoposide, bleomycin). The 4-year event-free (EFS) rate was 73.3 percent and the overall survival (OS) rate was 87.9% among patients with testicular GCT <sup>15</sup>.

**Conclusion:** The site of primary disease plays a role in the prognosis of pediatric germ cell tumors with the extra gonadal pelvic tumors being the worst regarding resectability. [it's not the same police](#). In the current study, the general outcome was good in terms of complete excision in most of the patients. Worst outcome noted in yolk sac tumor. There was a minimal recurrence rate.

References

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1. Pierce JL, Frazier AL, Amatruda JF. Pediatric germ cell tumors: a developmental perspective. *Advances in Urology*. 2018 Feb 4; 2018.
2. Fetcko K, Dey M. Primary central nervous system germ cell tumors: a review and update. *Medical research archives*. 2018 Mar; 6(3).
3. Calaminus G, Schneider DT, von Schweinitz D, Jürgens H, Infed N, Schönberger S, Olson TA, Albers P, Vokuhl C, Stein R, Looijenga L. Age-dependent presentation and clinical course of 1465 patients aged 0 to less than 18 years with ovarian or testicular germ cell tumors; data of the MAKEI 96 protocol revisited in the light of prenatal germ cell biology. *Cancers*. 2020 Mar; 12(3):611.
4. Schneider DT, Terenziani M, Cecchetto G, Olson TA. Gonadal and extragonadal germ cell tumors, sex cord stromal and rare gonadal tumors. In *Rare tumors in children and adolescents 2022* (pp. 301-389). Springer, Cham.
5. Shaikh F, Murray MJ, Amatruda JF, Coleman N, Nicholson JC, Hale JP, Pashankar F, Stoneham SJ, Poynter JN, Olson TA, Billmire DF. Paediatric extracranial germ-cell tumours. *The Lancet Oncology*. 2016 Apr 1; 17(4):e149-62.
6. Rescorla FJ. Pediatric germ cell tumors. In *Seminars in pediatric surgery* 2012 Feb 1 (Vol. 21, No. 1, pp. 51-60). WB Saunders.
7. Schneider DT, Calaminus G, Reinhard H, Gutjahr P, Kremens B, Harms D, Göbel U. Primary mediastinal germ cell tumors in children and adolescents: results of the German cooperative protocols MAKEI 83/86, 89, and 96. *Journal of clinical oncology*. 2000 Feb 14; 18(4):832-.

8. Newton C, Murali K, Ahmad A, Hockings H, Graham R, Liberale V, Sarker SJ, Ledermann J, Berney DM, Shamash J, Banerjee S. A multicentre retrospective cohort study of ovarian germ cell tumours: evidence for chemotherapy de-escalation and alignment of paediatric and adult practice. *European Journal of Cancer*. 2019 May 1; 113:19-27.
9. Fakhr IM, Khalil EA, El-Baradie TS, Shaalan MA, Shalaby LM, Nassif SL, Farahat IG. The role of surgical management in pediatric germ cell tumors (GCTs), NCI case series. *J Egypt Natl Canc Inst*. 2008 Mar 1; 20(1):70-9.
10. Nasir IU, Ashraf MI, Ahmed N, Shah MF, Pirzada MT, Syed AA, Qazi AQ. Clinical profile, treatment and survival outcomes of paediatric germ cell tumours: a Pakistani perspective. *Editorial Board*. 2016 Oct 1; 6:119.
11. Lin X, Wu D, Zheng N, Xia Q, Han Y. Gonadal germ cell tumors in children: A retrospective review of a 10-year single-center experience. *Medicine*. 2017 Jun; 96(26).
12. Laohverapanich K, Buaboonnam J, Vathana N, Sanpakit K, Takpradit C, Narkbunnum N, Pongtanakul B, Sowithayasakul P, Phuakpet K. Clinical Outcomes of Extracranial Germ Cell Tumors: A Single Institute's Experience. *Siriraj Medical Journal*. 2021 Oct 1; 73(10):680-6.
13. Agarwala S, Mitra A, Bansal D, Kapoor G, Vora T, Prasad M, Chinnaswamy G, Arora B, Radhakrishnan V, Laskar S, Kaur T. Management of pediatric malignant germ cell tumors: ICMR consensus document. *The Indian Journal of Pediatrics*. 2017 Jun; 84(6):465-72.

14. Ahmad A, Saleem M, Khan FS. Treatment outcome of prepubertal gonadal tumors. *Journal of Fatima Jinnah Medical University*. 2019 Apr 30; 13(1):07-11.
15. Kumar H, Saju SV, Radhakrishnan V, Raja A, Ganesan TS, Dhanushkodi M, Kalaiarasi JP, Mehra N, Joshi A, Rajan AK, Selvarajan G. Analysis of extra-cranial germ cell tumors in male children: Experience from a single centre in India. *Pediatric Hematology Oncology Journal*. 2020 Jun 1; 5(2):37-42.