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Original Article

# Germ Cell Tumors in Children: A Retrospective Review of a 04-Year Single-Center Experience

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## Abstract

**Introduction** Pediatric germ cell tumors (GCTs) are rare neoplasms that can be benign or malignant and occur in children and adolescents. They can arise from germ cells in the extragonadal or gonadal sites and have numerous histologic subtypes. The International Germ Cell Cancer Cooperative Group classification is used to guide treatment, with most children experiencing excellent overall survival (OS). Chemotherapy is historically recommended for all malignant GCTs. Nevertheless, surgery and observation alone may be sufficient for stage I gonadal GCTs. Using chemotherapy can lead to successful salvage of relapses..

**Objectives** Our institute has conducted a study with the objective of evaluating a group of 97 patients diagnosed with GCTs, who received treatment within the past 4 years.

**Materials and Methods** From January 2018 to April 2022, a total of 97 pediatric patients diagnosed with GCTs underwent surgical treatment at Indus Hospital & Health Network. The diagnosis was established by considering clinical features, tumor marker levels, imaging, and histology. Treatment was determined based on the risk stratification utilizing the United Kingdom Children's Cancer Study Group GC 2005–04 protocol. Patients classified as LR (low-risk) received chemotherapy only if a recurrence occurred after the initial surgery. On the other hand, IR (intermediate-risk) and HR (high-risk) patients received four and six cycles of JEB (chemotherapy regimen), respectively, followed by surgery. Recurrence was closely monitored through suspicion, tumor marker levels, or imaging. Patients experiencing a recurrence after JEB chemotherapy were treated with TIP (paclitaxel, ifosfamide, and cisplatin) chemotherapy and subsequently underwent surgery.

**Results** In this retrospective study, a group of 97 patients diagnosed with GCTs was analyzed. The cohort included 59 gonadal tumors and 38 extragonadal tumors. The most common histopathological types observed were yolk sac tumor and dysgerminoma. Out of the patients, 33 (34%) were classified as HR, 35 (36.1%) as IR, and 29 (29.9%) as LR. Among the patients, 16 experienced recurrence, while the remaining 90 patients (92.8%) were alive at the time of the analysis. The study determined the 5-year

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- germ cell tumors (GCT)
- children
- gonadal
- yolk sac tumor
- overall survival
- event-free survival

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event-free survival (EFS) rate as 83.5% and the OS rate as 92.8%. The presence of residual disease was found to be the only significant factor that influenced EFS.

**Conclusion** To manage GCTs in children, a multidisciplinary approach involving surgeons, oncologists, and radiation therapists is required. Surgery and chemotherapy have improved outcomes for children with GCTs, but personalized treatment planning is crucial. With advancements in pediatric oncology care, the prognosis for children with GCT in Pakistan has improved, providing hope for better outcomes in the future.

## Introduction

Pediatric germ cell tumors (GCTs) are rare tumors. GCTs originate from aberrant differentiation of germ cells and encompass a heterogeneous collection of neoplasms, exhibiting notable variations in histological characteristics and site of occurrence.[1,2] Children and adolescents can exhibit both benign and malignant GCTs, and the incidence rates of these tumors vary depending on their age.[3]

The overall incidence of GCTs in children up to 15 years of age can be estimated at 0.9 per 100,000 children.[1,3] In infants, majority are benign GCTs, with the most common site being sacrococcygeal. GCT accounts for 2 to 3% of all pediatric malignancies.[3] Out of all pediatric GCTs, approximately 60% originate from extragonadal sites, such as the mediastinum, pineal and sacrococcygeal regions, and retroperitoneum. On the other hand, the remaining 40% of cases are attributed to GCTs arising from the gonadal sites, specifically the ovary and testis.[4,5] GCTs are the most frequently occurring tumors in the gonads among children and adolescents.[6] While GCTs may exhibit notable variations depending on their anatomical location, they possess a significant degree of similarity and are generally regarded as a cohesive group.[1] GCTs shows a wide range of histologic subtypes. The histologic characteristics of each subtype are not influenced by the clinical presentation. However, the behavior of the tumor and its biological attributes vary based on factors such as the site of origin, stage of the tumor, and age of the patient.[7]

The International Germ Cell Cancer Cooperative Group (IGCCCG) classification is globally employed to identify patients at high risk (HR) and provide guidance for first-line treatment.[8] As per this classification, patients diagnosed with non-germinomatous GCTs or those with elevated levels of tumor markers are categorized as HR individuals.

The majority of children diagnosed with GCTs achieve remarkable overall survival (OS) rates, which has consequently resulted in a reduction in the extent of chemotherapy administered.[9] In the past, chemotherapy was typically advised for all cases of malignant GCTs. Nevertheless, research has demonstrated that stage I gonadal GCTs can be effectively managed with surgical intervention and close monitoring, without the need for additional therapy in many patients. Even in cases of relapse, chemotherapy has proven highly successful in salvaging the patients.[10,11]

To gain deeper insights into the clinical features and treatment approaches for pediatric GCTs, we conducted a comprehensive analysis of a cohort consisting of 97 patients with GCTs who were treated at our institution over the past 4 years.

## Materials and Methods

During the period spanning from January 2018 to April 2022, a group of 97 pediatric patients (16 years old or younger) diagnosed with GCTs received surgical treatment at the Indus Hospital & Health Network. The hospital's electronic database was utilized to gather comprehensive information including clinical records, radiological data, laboratory results, and pathological findings.

The diagnosis of GCTs was established by considering various factors, including clinical manifestations, elevated levels of tumor markers (such as serum α-fetoprotein [AFP] and β human chorionic gonadotropin [β-HCG]), imaging studies, and histological analysis. Each patient underwent contrast-enhanced computed tomography scans of the chest, abdomen, and pelvis. For pelvic tumors, magnetic resonance imaging of the pelvis with contrast was performed. Additionally, bone scintigraphy was conducted for staging purposes.

The United Kingdom Children's Cancer Study Group GC 2005–04 protocol was employed for both staging and treatment purposes. Patients were categorized into three risk groups: low risk (LR), intermediate risk (IR), and HR, based on their stage and prognostic factors. Patients classified as HR included those with AFP levels greater than 10,000 ng/mL, stage IV disease (excluding testis $<5$ years and all germinomas), or stage II to IV mediastinal tumors. For stage I tumors (LR), chemotherapy was administered only if there was disease recurrence following surgery. IR and HR patients received first-line chemotherapy consisting of four and six cycles of JEB (carboplatin 600 mg/m$^2$ on day 2, etoposide 120 mg/m$^2$ for 3 days, and bleomycin 15 mg/m$^2$ on day 3), respectively, followed by surgical intervention. Tumor markers were monitored to assess treatment response. After completing the initial treatment, all patients underwent long-term surveillance to detect any recurrence of the disease. In cases where patients experienced a recurrence after JEB chemotherapy, they received four cycles of second-line chemotherapy known as TIP (paclitaxel 175 mg/m$^2$ on day 1,

ifosfamide 1500 mg/m$^2$ from day 2 to 6 , cisplatin 20 mg/m$^2$ from day 2 to 6) followed by surgery.

The patients were closely monitored to assess their event-free survival (EFS) and OS rates. An "event" was defined as disease relapse/progression or death from any cause. EFS was determined by calculating the time from the start of treatment to the occurrence of the event, while OS was calculated from the start of treatment to the date of the last follow-up or date of death. In survival analysis, all patients were considered until the date of the last follow-up or until April 30, 2022, whichever came earlier.

### Primary Outcome

In this study, EFS and OS were the primary outcomes.

### Secondary Outcome

Most of the tumor recurrences occurred in the HR group of GCT and was found as an additional information.

### Inclusion Criteria

1. Patients with biopsy-proven extracranial GCTs within the age range of 0 to 16 years.
2. Patients who received surgical treatment outside of our hospital were also included.

### Exclusion Criteria

1. Patients older than 16 years were excluded.
2. Patients with intracranial GCTs.
3. Patients with refractory or progressive extracranial GCT treated outside of our institution.

## Statistical Analysis

The data analysis was performed using the Statistical Package for Social Sciences (SPSS; IBM, version 24.0, Armonk, New York, United States). For age, AFP, HCG, and lactate dehydrogenase (LDH) variables, the median (interquartile range) was calculated as the data did not follow a normal distribution. Frequencies and percentages were calculated for sex, histology, stage of the disease, presence of metastatic disease, initial treatment characteristics, recurrence, and outcomes. The frequency distributions along with corresponding percentages were also calculated for the categories of age, AFP, β-HCG, and LDH. A chi-square test/Fisher's exact test was run to check the association of outcome and recurrence of disease with demographic, laboratory, and clinical parameters. The Mann–Whitney test was employed to assess the median difference in AFP, β-HCG, and LDH values. The Kaplan–Meier method was utilized to estimate the OS and EFS rates. Univariate and multivariate analyses were conducted using Cox's proportional hazard model. The significant parameters identified in the univariate analyses were subjected to multivariate analysis, and their association with recurrence/outcome was expressed as hazard ratios (HRs) with a 95% confidence interval. A significance level of $< 0.05$ was set to determine a significant association between recurrence/outcome and the factors under investigation.

## Ethical Approval

This analysis was conducted under an ethical exemption granted by the institutional ethical review board with the reference IHHN_IRB_2022_07_020 on August 3, 2022. All procedures performed in the study involving human participants adhered to the ethical principles outlined by the institutional and/or national research committee. The study also complied with the guidelines set forth in the 1964 Helsinki Declaration and its subsequent amendments or equivalent ethical standards.

## Results

This retrospective study included a cohort of 97 patients, with a median age of 4 years (1.9–10) at the time of diagnosis. The male-to-female ratio was approximately 1:1.7, with males having a median age of 2 years (1.5–3.5) and females having a median age of 8.4 years (2.5–11).

According to the histopathology, the majority were the yolk sac tumor (YST) (50.5%), followed by dysgerminoma (17.5%). The study included a total of 97 patients, with 33 (34%) classified as HR, 35 (36.1%) classified as IR, and 29 (29.9%) classified as LR. The disease was metastasized in 28 (29%) patients, 17 (60.7%) had pulmonary metastatic diseases while 11 (39.3%) had nonpulmonary metastatic diseases at the time of diagnosis. The surgical excision was done in 84 (86.6%) patients, in which 55 (65%) had residual disease treated with adjuvant first-line chemotherapy and 29 (35%) were LR with complete surgical excision. The tumor was nonresectable in 13 (13.4%) patients, and neoadjuvant chemotherapy was given.

The first-line chemotherapy (JEB) was given to 68 (70%) patients. The recurrence has occurred in 16 patients in which 6 (38%) were from the LR group (chemo-naive) patients, 1 (6%) patient from IR, and 9 (56%) were from the HR group. The IR and HR patients were offered the second-line chemotherapy (TIP).

Out of the total patient population, 90 (92.8%) were reported as alive, while 7 patients (7.2%) had unfortunately passed away; the nonsignificant association of recurrence and outcomes with demographic, clinical, and laboratory parameters are depicted in ►**Table 1**.

There were 59 (60.8%) gonadal and 38 (39.2%) extragonadal GCTs. The anatomical distribution is shown in ►**Fig. 1A**, in which the common site of extragonadal was the abdomen, 14 (36.8%), followed by the sacrococcygeal, 13 (34.2%), while other 11 (29%) were the mediastinum and retroperitoneum sites. In the 13 sacrococcygeal region, 5 (38%) showed mature teratoma (MT), the age of these 5 patients were: 1 (20%) was $< 1$ year, 3 (60%) were $< 5$ years, and 1 (20%) patient was of 11 years.

In gonadal GCT, in testis, the most common was YST, 21 (80.8%), followed by mixed GCT (MGCT) 3 (11.5%) and each of one case of mature and immature teratoma (IMT). In ovarian tumor, dysgerminoma, 14 (42.4%), was the most common, followed by YST 8 (24.2%), MGCT 6 (18.2%), 1 (3%) MT, and two of each case of embryonal carcinoma (EC) and IMT.

 

**Table 1** Demographic, clinical, and laboratory parameters in study patients

| Characteristics | Recurrence | | *p*-Value | Outcomes | | *p*-Value |
|---|---|---|---|---|---|---|
| | Yes ($n=16$) | No ($n=81$) | | Alive ($n=90$) | Expired ($n=7$) | |
| Age (y) (*n*) (%) | | | | | | |
| < 10<br>> 10 | 13 (81.3)<br>03 (18.8) | 56 (69.1)<br>25 (30.9) | 0.385[a] | 63 (70)<br>27 (30) | 06 (85.7)<br>01 (14.3) | 0.669[a] |
| Sex (*n*) (%) | | | | | | |
| Male<br>Female | 04 (25)<br>12 (75) | 31 (38.3)<br>50 (61.7) | 0.312[b] | 32 (35.6)<br>58 (64.4) | 03 (42.9)<br>04 (57.1) | 1.000[a] |
| Histology (*n*) (%) | | | | | | |
| Mature teratoma | 01 (6.3) | 10 (12.3) | 0.685[a] | 11 (12.2) | 0 | 1.000[a] |
| Immature components (teratoma) | 01 (6.3) | 04 (4.9) | 1.000[a] | 05 (5.6) | 0 | 1.000[a] |
| Dysgerminoma | 02 (12.5) | 15 (18.5) | 0.730[a] | 16 (17.8) | 01 (14.3) | 1.000[a] |
| Mixed GCT | 03 (18.8) | 09 (11.1) | 0.412[a] | 11 (12.2) | 01 (14.3) | 1.000[a] |
| Yolk sac tumor | 09 (56.3) | 40 (49.4) | 0.616[b] | 44 (48.9) | 05 (71.4) | 0.436[a] |
| Embryonal carcinoma | 0 | 03 (3.7) | 1.000[a] | 03 (3.3) | 0 | 1.000[a] |
| Risk (*n*) (%) | | | | | | |
| Low risk<br>Intermediate risk<br>High risk | 06 (37.5)<br>01 (6.3)<br>09 (56.3) | 23 (28.4)<br>34 (42)<br>24 (29.6) | 0.019[b] | 29 (32.2)<br>31 (34.4)<br>30 (33.3) | 0<br>04 (57.1)<br>03 (42.9) | 0.191[a] |
| Metastatic disease (*n*) (%) | | | | | | |
| Yes<br>No | 05 (31.3)<br>11 (68.8) | 23 (28.4)<br>58 (71.6) | 0.772[a] | 27 (30)<br>63 (70) | 01 (14.3)<br>06 (85.7) | 0.669[a] |
| AFP (ng/mL) (*n*) (%) | | | | | | |
| < 10,000<br>> 10,000<br>Normal | 03 (18.8)<br>10 (62.5)<br>03 (18.8) | 28 (34.6)<br>30 (37)<br>23 (28.4) | 0.164[b] | 29 (32.2)<br>35 (38.9)<br>26 (28.9) | 02 (28.6)<br>05 (71.4)<br>0 | 0.169[a] |
| HCG (IU/L) (*n*) (%) | | | | | | |
| < 5,000<br>> 5,000 | 14 (87.5)<br>02 (12.5) | 73 (94.8)<br>04 (5.2) | 0.274[a] | 80 (92.9)<br>06 (7.1) | 07 (100)<br>0 | 1.000[a] |

Abbreviations: AFP, α-fetoprotein; GCT, germ cell tumor; HCG, human chorionic gonadotropin.
*Significant value.
[a]Fisher's exact test.
[b]Pearson's chi-square test.

Total 49 cases of YST were reported in our study, the AFP level was high ≥ 10,000 (ng/mL) in 34 (69.4%), < 10,000 (ng/mL) were 13 (26.5%), and 2 (4.1%) were in normal range.

The histopathological distribution is shown in ►**Fig. 1B**, YST and dysgerminoma were commonly found in 49 and 17 patients, respectively. MT and IMT were in 11 and 5 patients, respectively, however, 3 were EC.

MGCT was found in 12 patients; we have reported 3 patients in each MGCT with EC + YST and IMT + EC + YST. Two patients in each MGCT with YST + dysgerminoma, YST + IMT, and YST + MT. One in each MGCT with IMT + dysgerminoma (►**Fig. 1B**).

## Survival Analysis

The study followed all patients for a median duration of 17.2 months (8.2–25.3). Seven patients died, 03 were related to progressive disease, 01 had secondary malignancy (brain tumor), 02 had bacterial and fungal infections, and 01 patient had a recurrence of the disease.

Recurrence has occurred in 16 patients in which 10 (62.5%) were off treatment after first-line chemotherapy and 06 (37.5%) were LR chemo-naive patients. In these 6 patients, 1 had lymphovascular invasion and 2 patients had mixed histology, while 3 had dysgerminoma and 1 YST.

For the entire patient cohort ($n=97$), the 5-year EFS rate was determined to be 83.5%, while the 5-year OS rate was calculated as 92.8% (►**Fig. 2A**).

►**Fig. 2B** shows the 5-year EFS rates among different risk groups (LR, IR, and HR), demonstrating a statistically significant difference. Owing to female predominance and primary nononcological surgeries outside the tertiary care center, we found lower EFS in the LR group as compared with the IR group.

Furthermore, ►**Fig. 2C** illustrates the EFS rates for children without metastases (84.1%) and those with metastases

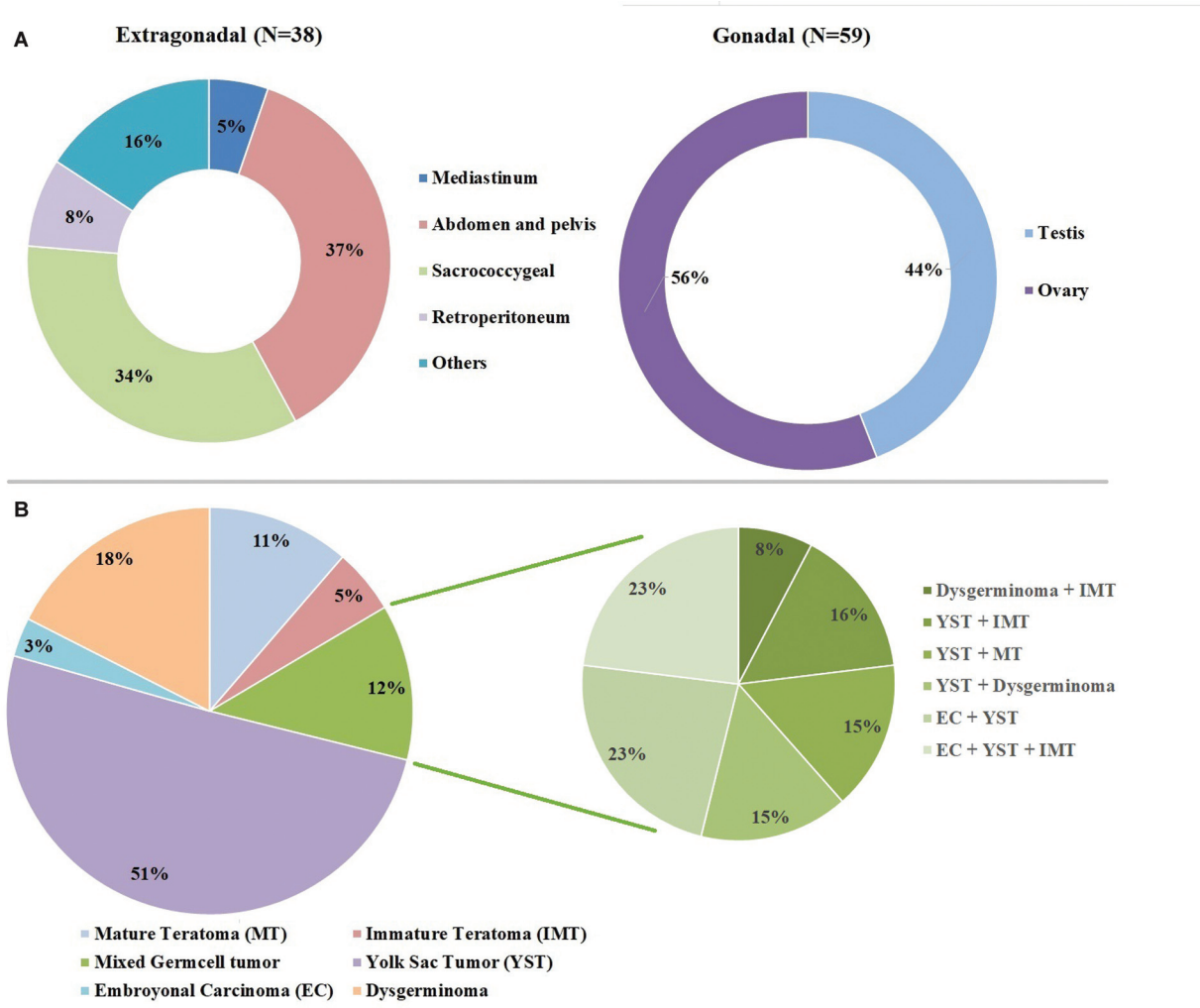


**Fig. 1** (A) Anatomical distribution of gonadal and extragonadal germ cell tumors. (B) Distribution according to histopathology.

(82.1%), showing no statistically significant difference. In ►**Fig. 2D**, patients with AFP < 10,000 ng/mL exhibited a higher EFS compared with those with elevated AFP ≥ 10,000 ng/mL, although the difference was not statistically significant. The EFS of patients after the first-line treatment with the small residual disease was 42.1% as compared with patients with complete remission, 93.6%, which was statistically significant (►**Fig. 2E**). Through multivariable analysis, it was determined that the presence of residual disease emerged as the sole independent prognostic factor, with a HRs of 7.42. The residual disease was small in size and was not amenable for surgery without mutilation. We did not encounter condition like growing teratoma syndrome. Also, patients in the HR group and AFP level > 10,000 ng/mL were found to have 2.4 and 1.3 times higher HRs, respectively, which was statistically nonsignificant. There were 36% higher chances of patients with metastatic disease to have disease recurrence, but it was statistically nonsignificant (►**Table 2**).

## Discussion

GCTs are uncommon neoplasms characterized by diverse histological subtypes, encompassing both benign and malignant forms. Due to their rarity, a retrospective study was conducted to evaluate the treatment outcomes of pediatric GCTs at our medical facility. Consistent with established international guidelines, all patients received chemotherapy as part of their treatment regimen.[12] In our study, girls were more frequently affected than boys, which is consistent with the literature.[13,14]

Malignant testicular tumors are less frequently reported compared with extragonadal GCTs and mature teratomas.[15] In our study, the majority of cases (60.8%) exhibited gonadal involvement, while 39.2% showed extragonadal involvement. Among the histological subtypes, YST was the most frequently observed, which aligns with findings from previous studies.[14,15] However, our study revealed that ovarian GCTs accounted for a larger proportion (56%) of the cases.

In our study, we also identified MGCTs, with the most prevalent combination being YST and EC. This finding is consistent with previous studies that have reported similar results, indicating the recurrent occurrence of this specific combination in MGCTs.[16] Tumor markers play a crucial role in the diagnosis, detection of relapse, and follow-up of GCTs. In our study, we found that serum

 

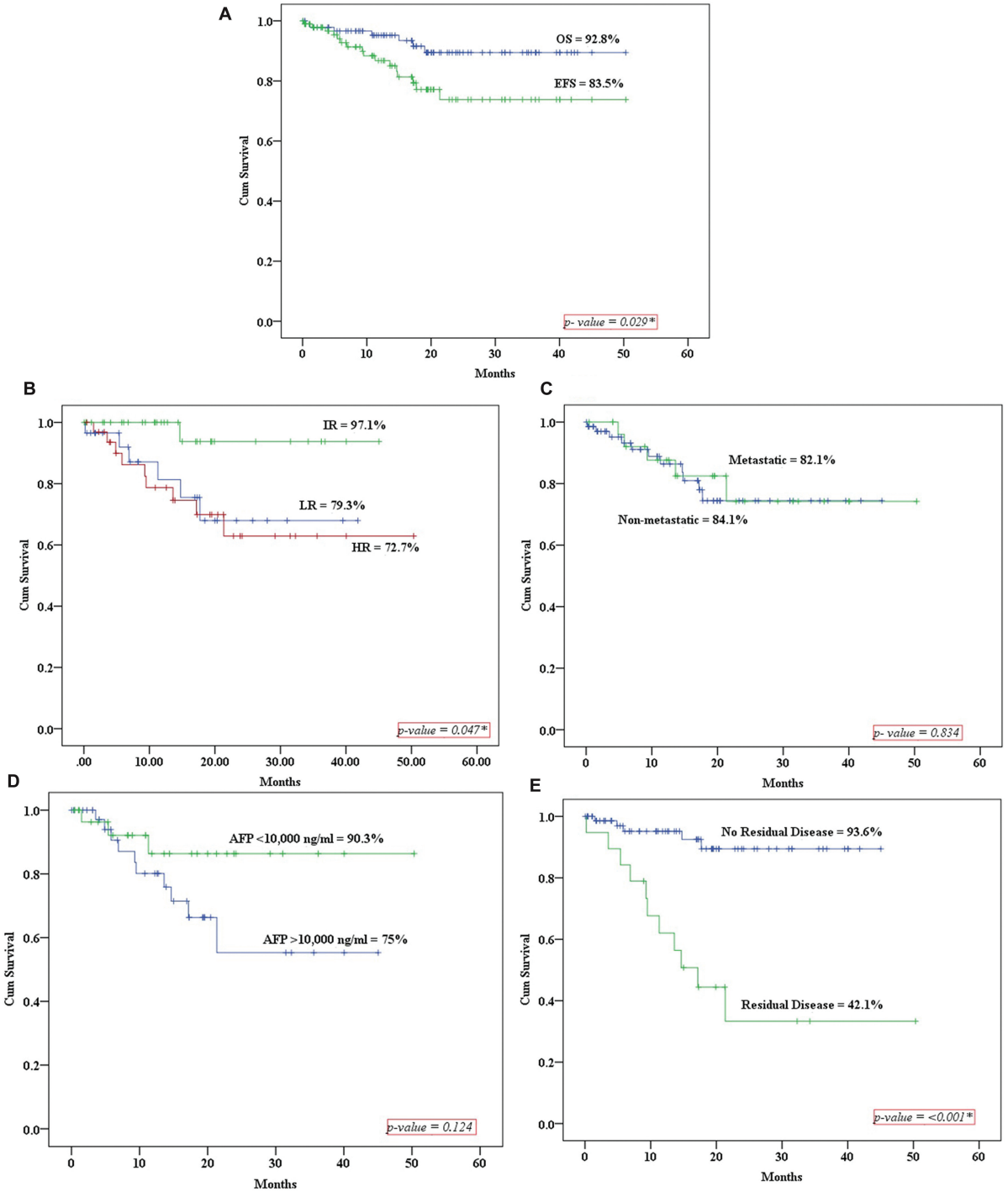


**Fig. 2** (**A**) The 5-year event-free survival (EFS) and overall survival (OS). (**B–E**) The 5-year EFS according to the risk factors (IR = intermediate risk; LR = low-risk; HR = high-risk; AFP = α-fetoprotein.).

AFP elevation, which is commonly associated with the presence of a YST component, was observed in 87.5% of patients with GCTs. These findings align with the results reported by Kumar et al, indicating a high concurrence in the incidence of elevated AFP levels among patients with GCTs.[16] Among the cases of YST in our study, 35 individuals (71.4%) exhibited an AFP level exceeding 10,000 ng/mL. Interestingly, our study did not identify elevated AFP as a significant prognostic factor, which aligns with the findings of a study conducted by Marina et al. This suggests that AFP levels may not independently predict the prognosis of YSTs in pediatric patients, consistent with the previous research.[17]

In our study, patients with β-HCG levels below 5,000 IU/L experienced a recurrence rate of 87.5%, with 92.9% of these patients still alive. In contrast, those with β-HCG levels above 5,000 IU/L had a recurrence rate of 12.5%, with only 7.1% alive. These findings are consistent with previous research that

**Table 2** Multivariate analysis for hazard ratio

| | HRs | 95% CI | *p*-Value |
|---|---|---|---|
| High-risk group | 2.416 | 0.656–8.895 | 0.185 |
| Metastatic disease | 0.361 | 0.098–1.331 | 0.126 |
| AFP > 10,000 (ng/mL) | 1.370 | 0.424–4.422 | 0.598 |
| Residual diseases | 7.426 | 2.455–22.46 | < 0.001[a] |

Abbreviations: AFP, α-fetoprotein; CI, confidence intervals; GCT, germ cell tumor; HR, hazard ratio.
[a]Significant value < 0.05.

identifies β-HCG as a significant prognostic marker in GCTs. For example, Lorch et al[18] demonstrated that elevated β-HCG levels in patients with metastatic GCTs were associated with poorer survival outcomes and a higher likelihood of recurrence.

The management approach for GCTs is influenced by various factors such as tumor location, disease extent, patient age, and coexisting medical conditions. Typically, the management strategy involves surgical resection for localized disease, chemotherapy for cases with residual or metastatic disease, and a combination of neoadjuvant chemotherapy and delayed surgical excision for unresectable lesions. These treatment modalities are implemented based on individual patient considerations to optimize outcomes in GCT management.[19,20] Localized GCTs are primarily treated through surgical resection. The primary objective of the surgical procedure is to achieve complete removal of the tumor while ensuring the preservation of normal tissue and organ function. The surgical approach aims to maximize tumor removal while minimizing potential damage to surrounding healthy tissues and organs. In some cases, a radical orchiectomy (removal of the testicle) may be necessary for testicular GCTs. In ovarian GCTs, surgical resection may involve removal of the affected ovary or ovaries.[19,20] Chemotherapy is the primary treatment for residual or metastatic disease. Platinum-based chemotherapy, which includes drugs such as cisplatin, carboplatin, and oxaliplatin, has been shown to be highly effective in treating GCTs. Chemotherapy is typically given in cycles, with a period of rest between each cycle to allow the body to recover.[19,20] Unresectable lesions in GCTs may be managed through a combination of neoadjuvant chemotherapy and delayed surgical excision. Neoadjuvant chemotherapy refers to the administration of chemotherapy before surgery, with the goal of reducing the size of the tumor and increasing the feasibility of surgical removal. This approach allows for tumor shrinkage, facilitating subsequent surgical intervention by improving the chances of achieving complete resection while preserving normal tissue function. Neoadjuvant chemotherapy followed by delayed surgical excision is employed to optimize the management of GCTs in cases where immediate surgical resection is not feasible. Delayed surgical excision involves waiting until the tumor has responded to chemotherapy before removing it surgically.

The introduction of platinum-based chemotherapy has led to a remarkable improvement in the chances of survival for children diagnosed with GCTs. Currently, approximately 90% of children with GCTs can expect to survive for at least 5 years, a substantial increase compared with the less than 50% survival rate in the period before platinum-based treatments were available. Nevertheless, the outlook for each child is influenced by various factors such as the specific type and location of the tumor, the stage of the disease at diagnosis, as well as the age and overall health of the patient.[19,20]

Our study revealed consistent findings with regard to the cure rates of ovarian and testicular GCTs at different stages. Specifically, stage I GCTs exhibited a 100% cure rate, indicating successful treatment for all patients in this stage. For stage III GCTs originating from any primary site, the cure rate was determined to be 82%, while for stage IV GCTs from any primary site, the cure rate stood at 75%. Furthermore, we observed that the histology, or tumor type, played a significant role in prognosticating immature malignant teratoma ovarian tumors. Among these ovarian tumors, those of the neural type with grades II and III demonstrated the least favorable prognosis.[21,22] Two cases of ovarian tumors with progressive disease were identified in our report. Unfortunately, these patients were lost to follow-up after undergoing second-line chemotherapy.

A study conducted by Akyüz et al[23] from Turkey reported the OS and EFS rates in ovarian tumors as 68 and 57%, respectively, but in our study, we reported 97% OS and 84.8% EFS in ovarian tumors. We have 96.6% OS for gonadal tumors and 86.8% for extragonadal tumors; however, in a study conducted by Feltbower et al,[24] the 5-year survival rates for gonadal GCT were reported to be 93 to 95%, while the rates for extragonadal GCT were 70 to 75%. Mann et al[25] also reported similar findings, with 5-year survival rates of 90.9 and 87.8%, which aligned with our study. Furthermore, a more recent extensive population-based study from Germany indicated a 5-year survival rate of 92% for both gonadal and extragonadal GCTs.[26]

Risk of recurrence is more in patients with HR disease as we reported in our study, 27.3% in HR. Actual recurrence occurred more in patients with residual disease after first-line chemotherapy, that is, 55.6%, rather than patients with no residual.

Pediatric and adult GCTs have many differences in terms of histology, different staging systems, and survival. In adult gonadal GCT, testicular GCT is staged as per the American Joint Committee on Cancer and ovarian as per the International Federation of Gynecology and Obstetrics, while pediatric GCT as per the IGCCCG.[27] MGCTs are more common in adolescent and young adults. Children with testicular non-seminomatous GCT have improved survival compared with adults.[28]

 

The study provides confirmation that positive outcomes can be attained for children diagnosed with pediatric GCTs. It highlights the significant impact of a multidisciplinary approach to pediatric oncology care, which has substantially enhanced survival rates for children with GCTs in Pakistan. The recent advancements in health care services within the country have played a crucial role in raising life expectancy and achieving better outcomes for children with cancer.

## Study Limitations

We have presented in this study the in-depth analysis of GCTs but our data has some limitations. We were not able to do follow-up of this large cohort for short duration, so far. We aim to follow this cohort with longer duration and add assessment of long-term toxicities of chemotherapy.

## Conclusion

In conclusion, a comprehensive approach involving collaboration among surgeons, histopathologists, oncologists, and radiation therapists is crucial for effectively managing GCTs in children. The combination of surgical interventions and chemotherapy has played a vital role in enhancing the overall outcomes for pediatric GCT patients. However, it is essential to develop personalized treatment plans to maximize the effectiveness of interventions. With the continuous advancements in pediatric oncology care, there has been a notable improvement in the prognosis for children with GCTs in Pakistan, instilling optimism for even better outcomes in the future.

### Patients Consent

Informed patient consent was obtained for this study.

### Funding

None.

### Conflict of Interest

None declared.

### Acknowledgment

None.

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