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## Research Article

# Clinical Features and Treatment Outcomes in Patients with Extracranial Germ Cell Tumors: A Tertiary Centre Experience

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## ABSTRACT

**Background:** Germ cell tumors are histologically heterogeneous group of tumors with high cure rate if diagnosed early. The aim of study was to evaluate the extracranial germ cell tumors presenting to our institute with regards to gender, age, clinical presentation, pathology, management, acute toxicity and survival.

**Material and Methods:** This retrospective study was conducted at Department of Radiation Oncology, All India Institute of Medical Sciences (AIIMS), Patna.

**Results:** Total of 75 patients with germ cell tumor (GCT) were analysed. Distribution of males and females were 50.7% and 49.3% respectively. The median age of presentation of males and females was 31 years and 15 years respectively. At the time of presentation, 47.3% male and 16.2% of female patients had metastatic disease. The median alpha-fetoprotein (AFP), beta subunit of human chorionic gonadotropin (βHCG), and lactate dehydrogenase (LDH) were 112 ng/ml, 668 mIU/ml, and 550 U/L respectively. At median follow-up of 34 months, 32% of the patient developed recurrence. The median disease-free survival (DFS) and overall survival (OS) were 57 months and 71 months respectively. Multivariate analysis showed that the histological subtypes ( $p = 0.001$ ) and risk groups ( $p = 0.029$ ) were the independent prognostic factors for DFS, while metastatic status at presentation ( $p = 0.037$ ), upfront surgical intervention ( $p = 0.039$ ), and histopathological subtypes ( $p = 0.009$ ) were the independent prognostic factor for OS.

**Conclusion:** GCT is primarily a disease of young and adolescents. Early diagnosis, well-orchestrated multidisciplinary management leads to favourable outcome and survival.

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## Introduction

Germ cell tumors (GCT) are a heterogeneous group of tumors, which are curable. They arise from primordial germ cells that migrate during embryogenesis from yolk sac to the gonads. They are broadly classified into gonadal and extragonadal based on anatomy. Again, it can be classified into the following groups depending on pathology.

- i. Teratoma,
- ii. Malignant germ cell tumor
- iii. Mixed GCT: a separate entity, which houses two different types

Teratoma can be divided into mature teratoma and immature teratoma. Malignant GCT is classified as seminomatous (ST) and nonseminomatous (NST) in males, dysgerminoma, and non-dysgerminomas in females that include yolk sac tumors, embryonal carcinoma, gonadoblastoma and choriocarcinoma.

Various registries throughout the world have different reported incidences of testicular GCT varying from 1.7 per 100,000 to 2.7 per 100,000 amongst males, from 15-39 years of age. The incidence is increasing according to many reports worldwide [1]. European Cancer

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Registry-Based Study on Survival and Care of Cancer Patients (EUROCARE) reports markedly distinct age-adjusted incidence rates of GCTs in Europe for males and females 64 per 1,000,000 versus 4 per 1,000,000, respectively. There is lack of Indian data. In general, 80% of GCT are benign, 20% are malignant. In the pediatric age group, 2.5% of malignant germ cell tumors are found [2]. Germ cell tumors usually occur in the second or third decade of life. Fertility sparing surgery is offered to all patients. Chemotherapy with platinum-based combinations has extended 5-year survival rates from 100 % in stage I to approximately 75% in higher stages. Despite good clinical outcome, in developing countries such as ours there are many challenges we come across while treating patients especially since they present with advanced stage, heavy nodal burden and poor risk factors. In this study, we report our experience of extracranial germ cell tumors at a tertiary referral center, focussing on demography, histopathology, management, outcome and prognosis.

## Aim

Aim of study was to evaluate the extracranial germ cell tumors presenting at our institute with regards to gender, age, clinical presentation, pathology, management, acute toxicity and survival.

## Materials and Methods

### I Patients

We conducted a tertiary hospital based retrospective study in the department of Radiation Oncology at AIIMS, Patna, wherein all cases of registered germ cell tumors during the period from August 2014 to March 2020 was retrieved from the recorded files and analysed. The study focused on demographic profile as well as clinical presentation with respect to age, presenting complaints, histological types and tumor markers, surgical procedures, systemic chemotherapy, toxicity and disease-free survival (DFS) and overall survival (OS) outcomes. A detailed history, physical examination, and performance status of all patients was recorded. Eastern Cooperative Oncology Group performance status (ECOG PS) scale was used for performance status. Radiological investigations included a contrast-enhanced computed tomography (CECT) of abdomen, pelvis and thorax in majority of the cases. Ultrasonography of the abdomen and chest x-ray was also done for some patients. Magnetic resonance imaging (MRI) brain was done for symptomatic patients. Complete blood count (CBC), liver function test (LFT), kidney function test (KFT) were evaluated upfront. Tumor markers like alpha-fetoprotein (AFP), beta subunit of human chorionic gonadotropin ( $\beta$ HCG), and lactate dehydrogenase (LDH) was evaluated for every patient initially and also during therapy. Pulmonary function test (PFT) was performed prior to start of chemotherapy in almost all patients. Sperm banking was offered to all adult male patients. Staging and risk categorization was done as per American Joint Committee on Cancer (AJCC) 7th edition and risk categorization on the basis of International Germ Cell Cancer Collaborative Group (IGCCCG) [3, 4].

A written informed consent was obtained prior to chemotherapy and surgery. Surgical procedures were evaluated. It was either biopsy initially to unilateral oophorectomy (fertility sparing surgery) or total abdominal hysterectomy and bilateral salpingo-oophorectomy in

females. In males, biopsy for upfront inoperable disease or high inguinal unilateral orchiectomy was the procedure performed. The tissues were evaluated primarily with hematoxylin and eosin stain; however, IHC was evaluated wherever needed. Patients were treated with the standard chemotherapy protocols. Patients warranting chemotherapy were put on BEP regimen (Bleomycin 30 units day 1, day 8, day 15, Etoposide 100 mg/m<sup>2</sup> and Cisplatin 20 mg/m<sup>2</sup> on day 1 to 5 every three weeks). Chemotherapy regimen was changed to EP (Etoposide 100 mg/m<sup>2</sup> and Cisplatin 20 mg/m<sup>2</sup> on days 1 to 5 every three weeks) after 4 cycles of BEP in patients who had indications for more than four cycles of chemotherapy. Bleomycin was omitted in patients with abnormal pulmonary function test. Chemotherapy was administered for 4-6 cycles in majority of the patients. Patients were reviewed for toxicities before every cycle of chemotherapy. Toxicity was evaluated according to National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE version 5.0) [5]. Response evaluation was done in all patients after three chemotherapy cycles and after completion of all defined cycles as per stage with tumor markers (AFP,  $\beta$ HCG and LDH), ultrasonography or CECT of the abdomen and pelvis.

### II Follow Up

All patients were advised three monthly follow up during the first 2 years followed by six monthly thereafter. Physical examination, marker evaluation as well as chest radiograph and CT scan of abdomen and pelvis were performed.

### III Evaluation

Complete remission was taken as normalisation of tumor markers and resolution of tumor mass on CT scan. Progressive disease were defined as rising markers post treatment normalisation, new lesion on radiological examination, and pathologically proven new lesion.

### IV Statistical Analysis

The Statistical Package for the Social Sciences (IBM SPSS version 25 for Windows) was used for statistical analysis. The descriptive statistics were used to characterize the patient population. Chi-square test and Kaplan Meier survival curves were plotted for disease-free survival (DFS) and overall survival (OS). Cox regression model was used for univariate analysis and multivariate analysis of prognostic factors. The prognostic factors having statistically significant p-value in univariate analysis were included in multivariate analysis. A p-value of < 0.05 considered statistically significant in all performed analysis. Disease-free survival was defined as time from diagnosis until recurrence (local or systemic) whereas overall survival was defined as time from diagnosis to death or last follow-up.

## Results

### I Patient's Characteristics

Total of 75 patients with germ cell tumor (GCT) were analysed, the distribution of males and females were 50.7% and 49.3% respectively. The median age of presentation of males and females were 31 years and 15 years respectively. In males (n=38) most common involved age group

was 31-40 years followed by 21-30 years, 11-20 years, 41-50 years, 1-10 years, and > 50 years as 31.6%, 28.9%, 10.5%, 10.5%, 10.5%, and 7.9% respectively. In females (n=37) most common involved age group was 11-20 years followed by 21-30 years, 1-10 years, 31-40 years, 41-50 years, and > 50 years as 62.2%, 16.2%, 13.5%, 2.7%, 2.7%, and 2.7% respectively. Epidemiological details are given in (Table 1). Most common presenting symptom was testicular mass followed by neck

node, hemoptysis, sacral mass, abdominal pain, abdominal pain and lump as 71.1%, 7.9%, 5.3%, 5.3%, 5.3%, and 5.3% respectively in males. In females' abdominal pain, abdominal pain and lump, sacral mass, shortness of breath, and bleeding per vagina were 45.9%, 40.5%, 5.4%, 5.4%, and 2.7% respectively. The ECOG PS 0, 1, 2, and 3 were 31.6%, 39.5%, 18.4%, and 10.5% respectively in males while in females were 18.9%, 35.1%, 35.1%, 10.8% respectively.

**Table 1:** Characteristics of patients of malignant germ cell tumors.

		Male (N=38)		Female(N=37)	
Characteristics		count	N %	count	N %
Age group	1 - 10 years	4	10.5%	5	13.5%
	11 - 20 years	4	10.5%	23	62.2%
	21 - 30 years	11	28.9%	6	16.2%
	31 - 40 years	12	31.6%	1	2.7%
	41 - 50 years	4	10.5%	1	2.7%
	> 50 years	3	7.9%	1	2.7%
ECOG PS	ECOG_0	12	31.6%	7	18.9%
	ECOG_1	15	39.5%	13	35.1%
	ECOG_2	7	18.4%	13	35.1%
	ECOG_3	4	10.5%	4	10.8%
Presenting complains	Abdominal pain	2	5.3%	17	45.9%
	Abdominal pain and lump	2	5.3%	15	40.5%
	Bleeding per vagina	0	0.0%	1	2.7%
	Hemoptysis	2	5.3%	0	0.0%
	Neck node	3	7.9%	0	0.0%
	Sacral mass	2	5.3%	2	5.4%
	Shortness of breath	0	0.0%	2	5.4%
	Testicular swelling	27	71.1%	0	0.0%
Diagnosis	Dysgerminoma	0	0.0%	17	45.9%
	Mediastinal germ cell tumor	0	0.0%	2	5.4%
	Non dysgerminoma	0	0.0%	16	43.2%
	Non seminoma	17	44.7%	0	0.0%
	Seminoma	19	50.0%	0	0.0%
	Sacroccygeal teratoma	2	5.3%	2	5.4%
Histological subtypes	Embryonal cell carcinoma	5	13.2%	3	8.1%
	Choriocarcinoma	1	2.6%	0	0.0%
	Immature teratoma	0	0.0%	5	13.5%
	Mature teratoma	0	0.0%	0	0.0%
	Mixed GCT	11	28.9%	3	8.1%
	Endodermal sinus / yolk sac tumor	2	5.3%	9	24.3%
	Seminoma	19	50.0%	0	0.0%
	Dysgerminoma	0	0.0%	17	45.9%
Metastasis	No metastasis	20	52.6%	31	83.8%
	Ascites	0	0.0%	4	10.8%
	Inguinal lymph nodes	2	5.3%	0	0.0%
	Liver	4	10.5%	1	2.7%
	Lung	9	23.7%	1	2.7%
	Supraclavicular lymph nodes	3	7.9%	0	0.0%
Metastasis at diagnosis	Yes	18	47.4%	6	16.2%
	No	20	52.6%	31	83.8%
S- group	S0	0	0.0%	0	0.0%
	S1	17	44.7%	18	48.6%
	S2	17	44.7%	16	43.2%
	S3	4	10.5%	3	8.1%
Risk group	Good	17	44.7%	18	48.6%

	Intermediate	13	34.2%	13	35.1%
	High	8	21.1%	6	16.2%
<b>Surgical details</b>	Biopsy	6	15.8%	4	10.8%
	Cytoreductive surgery	1	2.6%	3	8.1%
	Left high inguinal orchidectomy	11	28.9%	0	0.0%
	Left salpingo-oophorectomy	0	0.0%	12	32.4%
	Right high inguinal orchidectomy	20	52.6%	0	0.0%
	Right salpingo-oophorectomy	0	0.0%	12	32.4%
	TAH + BSO	0	0.0%	6	16.2%
<b>Upfront surgery</b>	Yes	32	84.2%	30	81.0%
	No	6	15.7%	7	18.9%
<b>Stage</b>	Stage I	5	13.2%	13	35.1%
	Stage II	14	36.8%	8	21.6%
	Stage III	19	50.0%	11	29.7%
	Stage IV	0	0.0%	5	13.5%
<b>Treatment defaulted</b>	Yes	7	18.4%	5	13.5%
	No	31	81.6%	32	86.5%

ECOG PS: Eastern Cooperative Oncology Group Performance Scale; S group: serum tumor marker group; GCT: germ cell tumor; TAH and BSO: total abdominal hysterectomy and bilateral salpingo-oophorectomy; BEP: bleomycin, etoposide, cisplatin.

At the time of presentation, 47.3% (18) males and 16.2% (6) of female patients had metastatic disease. The most common site of metastasis in males was lung followed by liver, supraclavicular lymph nodes, and inguinal lymph nodes as 23.7%, 10.5%, 7.9%, and 5.3% respectively. In females, the most common metastasis was ascites followed by liver and lung as 10.8%, 2.2% and 2.7% respectively. The median value at presentation of AFP,  $\beta$ HCG, and LDH were 66.5 ng/ml, 673 mIU/ml, and 557 U/L respectively in males and 152 ng/ml, 655 mIU/ml, and 458 U/L respectively in females. The overall median AFP,  $\beta$ HCG, and LDH were 112 ng/ml, 668 mIU/ml, and 550 U/L respectively. On risk group classification good risk, intermediate risk, and poor risk were 44.7%, 34.2%, and 21.1% respectively in males whereas 48.6%, 35.1%, and 16.2% respectively in females. Serum tumor markers group S1, S2, and S3 in males were 44.7%, 44.7%, and 10.5% whereas in females 48.6%, 43.2%, and 8.1% respectively. Most of the patients were considered for upfront surgical intervention. 84.2% (32) of males and 81.0% (30) of females underwent upfront surgery.

15.8% (6) of males and 19% (7) of females were considered for neoadjuvant chemotherapy (NACT) followed by surgical intervention. At presentation 81.5% (31) of male patients underwent high inguinal orchidectomy, debulking surgery in 2.6% (one patient with sacrococcygeal mass), whereas biopsy was performed in 15.8% (6). Surgical intervention in females included biopsy in 10.8% (4), cytoreductive surgery in 8.1% (3), fertility sparing surgery in 64.8% (24), total abdominal hysterectomy and bilateral salpingo-oophorectomy in 16.2% (6) patients. Postoperative staging revealed that 13.2%, 36.8%, and 50% were in stage I, stage II, and stage III respectively in males. In females 35.1%, 21.6%, 29.7%, and 13.5% were stage I, stage II, stage III, and stage IV respectively. Postoperatively 94.7% of male patients had chemotherapy whereas 94.6% of female patients had adjuvant chemotherapy. Pre-chemotherapy pulmonary function test (PFT) was done in 65.8%, not done in 10.5% while the status not known in 23.7% of male patients. In females 62.2% of patients underwent PFT, 18.9% did not undergo PFT while the status is not known of 18.9% of patients.

The median numbers of chemotherapy cycles were 4 (range 1-6) in both male and females. In all patients who received more than 4 cycles of chemotherapy, their chemotherapy regimen was changed to EP after four cycles of BEP. Post-chemotherapy toxicity analysis in males revealed that 42.1% developed mild grade I complications. Grade III toxicities including diarrhoea, mucositis, neutropenia, anaemia and febrile neutropenia was seen in 18.4%, 7.9%, 7.9%, 10.5% and 13.2% respectively.

In Females grade I toxicity was seen in 53% patients. Grade III diarrhoea, mucositis, neutropenia and febrile neutropenia was seen in 7.7%, 10.4%, 13.1% and 15.8% patients respectively. Post treatment the overall median value of AFP,  $\beta$ HCG, and LDH were 3 ng/ml, 2 mIU/ml, and 287 U/L respectively. In males the median post treatment AFP,  $\beta$ HCG, and LDH were 4.1 ng/ml, 2.9 mIU/ml, and 312 U/L respectively. In females post treatment AFP,  $\beta$ HCG, and LDH were 2.2 ng/ml, 1.4 mIU/ml, and 255 U/L respectively. Histopathological analysis grossly revealed that in males 44.7%, 50%, and 5.3% of cases were of non-seminoma, seminoma, and sacrococcygeal teratoma respectively. In females 45.9%, 43.2%, 5.4%, and 5.4% were dysgerminoma, non-dysgerminoma, sacrococcygeal teratoma, and mediastinal GCT respectively. Histopathological diagnosis along with immunohistochemistry in certain cases showed that seminoma, mixed GCT, embryonal cell carcinoma, endodermal sinus tumor/yolk sac tumor, and choriocarcinoma were 50%, 28.9%, 13.2%, 5.3%, and 2.6% respectively. Immunohistochemistry (IHC) reports were available 30.6% of patients. In female's dysgerminoma, endodermal sinus tumor/yolk sac tumor, immature teratoma, mixed GCT, embryonal cell carcinoma were 45.9%, 24.3%, 13.5%, 8.1%, and 8.1% respectively. The median value of maximum tumor size was 6 cm (3.2-12.3) in males and 9 cm (3.2-21.6) in females. Tumor details, serum tumor markers, and follow-up duration depicted in (Table 2).

**Table 2:** Details of tumor markers, tumor description, age, and follow-up.

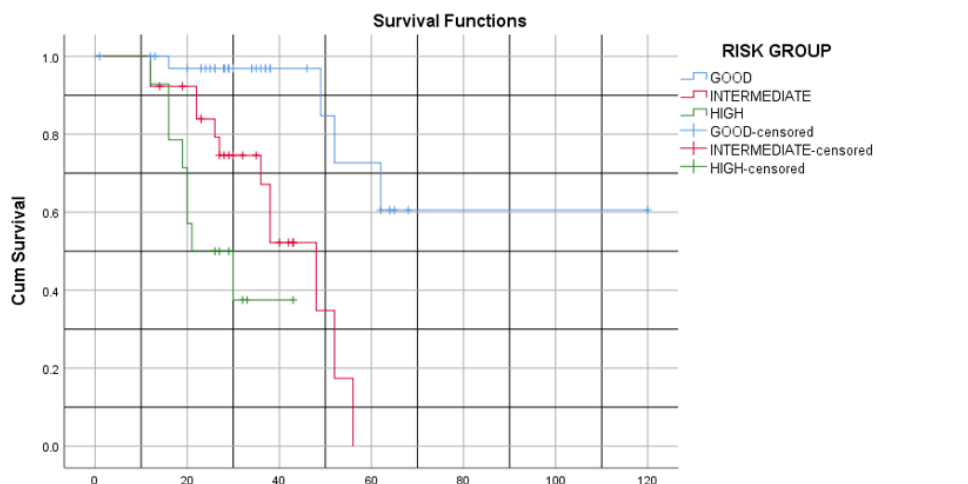
	Age (years)	Maximum size tumor (cm)	AFP	$\beta$ HCG	LDH	Follow up (months)
Male (N=38)						
Median	31.00	6.00	4.10	2.95	312.00	38.50
Minimum	1	3.20	0.10	0.20	143.00	1.00
Maximum	61	12.30	47.00	32.00	685.00	120.00
Female (N=37)						
Median	15.00	9.00	2.20	1.40	255.00	33.00
Minimum	2	3.20	0.10	0.01	168.00	17.00
Maximum	60	21.60	40.00	300.00	1718.00	81.00

AFP: alpha-fetoprotein;  $\beta$ HCG: beta subunit of human chorionic gonadotropin; LDH: lactate dehydrogenase.

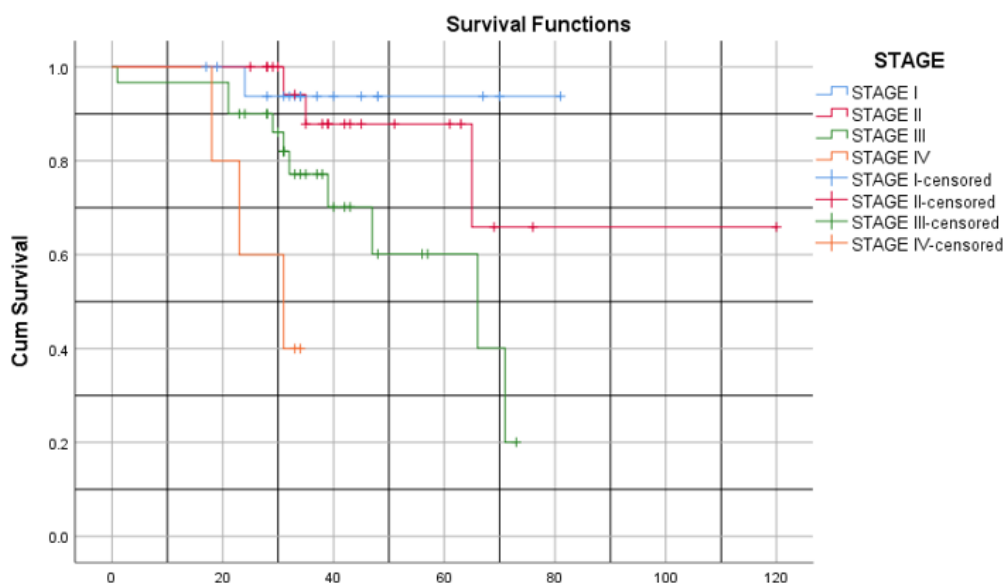
## II Survival Analysis

The median follow-up duration was 34 months (12-120). Twenty-four (32%) patients had a recurrence until last follow up in March 2020. The median DFS and OS were 57 months (95% CI: 51.826 - 62.174) and 71 months (95% CI: 67.475 - 74.525). In both groups the 3-year and 5-year DFS was 77.4% and 42.8% respectively whereas 3-year and 5-year OS

was 81.3% and 67% respectively. DFS was statistically significantly differing according to risk group (Log Rank:  $p < 0.001$ ) (Figure 1), histopathological subtypes (Log Rank:  $p < 0.001$ ), stage (Log Rank:  $p = 0.002$ ). OS was also statistically significantly differing according to risk group (Log Rank:  $p = 0.001$ ), histopathological subtypes (Log Rank:  $p < 0.001$ ), stage (Log Rank:  $p = 0.001$ ) (Figure 2).



**Figure 1:** Disease-free survival in months with risk group classification; Log Rank (Mantel Cox)  $p < 0.001$ .



**Figure 2:** Overall survival in months according to stage; Log rank (Mantel Cox)  $p = 0.001$ .

### III Analysis of Prognostic Factors

Univariate analysis using Cox-regression showed that histopathological subtypes, metastatic status at diagnosis, risk group, upfront surgery, stage were affecting the DFS and OS ( $p < 0.05$ ) in addition to that OS is also influenced by ECOG PS at diagnosis ( $p = 0.044$ ). Multivariate

analysis showed that the histological subtypes ( $p = 0.001$ ) and risk groups ( $p = 0.029$ ) are the independent prognostic factors for DFS, while metastatic status at presentation ( $p = 0.037$ ), upfront surgical intervention ( $p = 0.039$ ), and histopathological subtypes ( $p = 0.009$ ) were the independent prognostic factor for OS details depicted in (Table 3).

**Table 3:** Univariate and multivariate analysis of factors associated with disease-free survival (DFS) and overall survival.

Characteristics	Univariate analysis (DFS)			Multivariate analysis (DFS)		
	HR	95% CI	p-value	HR	95% CI	p-value
Metastatic status at diagnosis	6.436	2.357-17.573	< 0.001	1.112	0.260-4.905	0.871
Risk group	4.185	2.199-7.963	< 0.001	2.607	1.103-6.162	0.029
Upfront surgery	3.385	1.516-7.560	0.003	2.101	0.773-5.710	0.146
Stage	2.264	1.315-3.898	0.003	1.054	0.458-2.427	0.901
Histopathological subtypes	0.708	0.612-0.820	< 0.001	0.740	0.623-0.879	0.001
ECOG-PS	1.516	0.975-2.357	0.065			
Characteristics	Univariate analysis (OS)			Multivariate analysis (OS)		
	HR	95% CI	p-value	HR	95% CI	p-value
Metastatic status at diagnosis	17.477	3.836-79.626	< 0.001	8.825	1.144-68.064	0.037
Risk group	3.111	1.550-6.245	< 0.001	0.820	0.332-2.028	0.668
Upfront surgery	6.633	2.325-18.920	< 0.001	3.706	1.069-12.853	0.039
Stage	3.018	1.513-6.022	0.002	0.874	0.290-2.630	0.811
Histopathological subtypes	0.723	0.612-0.854	< 0.001	0.757	0.613-0.934	0.009
ECOG-PS	1.720	1.014-2.917	0.044	1.229	0.649-2.329	0.527

### Discussion

GCTs are uncommon tumor. The incidence of GCT is increasing. There is a lack of recent data from India on epidemiology of GCT. The male and female distribution was equal in our study. In this study, the median age at diagnosis was 31 years and 15 years in males and females. The findings from other Indian study by Joshi A *et al.* reported that the median age for seminomatous and nonseminomatous GCT were 28 years and 39 years respectively in males [6]. Mustafa SA *et al.* in their study reported that the median age was 37 years for males [7]. Lakshman M *et al.* in their study reported the median age of female GCT as 22 years [8]. In our study, we noted that the most commonly affected age group were 31-40 years in males and 11-20 years in females. This distribution was similar to study by SS Chavan *et al.* [9]. However, some studies reported the bimodal distribution of age [10]. Testicular mass and abdominal pain was the most common presenting symptoms in males and females respectively in our study. 47.3% and 16.7% were metastatic disease at presentation for males and females respectively. The most common metastatic site was lungs; other studies also reported findings to consistent with our study [6, 8].

Western literature reported the similar epidemiological findings to that of our study especially considering male patients with median age at diagnosis of 28 years, 56% of the male GCT patients were in metastatic stage [11]. In our study male patient were in good, intermediate, and poor risk as 44.7%, 34.2%, and 21.1% respectively and female patients on risk group stratification were in 48.6%, 35.1%, and 16.2% respectively. Vasconcellos *et al.* reported similar risk group distribution of patients for male GCT. The most common histological subtype was seminoma in males and dysgerminoma in females similar to other studies [6, 7, 10]. In this study seminoma and dysgerminoma was associated with raised

AFP and LDH, nonseminoma and non-dysgerminoma was associated with raised AFP,  $\beta$ HCG, and LDH, which was consistent with other aforementioned studies. The median number of chemotherapy cycles were 6 in both male and female patients. The median size of the tumor was 6 cm in males and 9 cm in females, which were consistent with other studies [6, 9]. The incidence of febrile neutropenia was less in this study, compared to study by Joshi *et al.* This may be due to prophylactic use of GCSF in our study. The median delay due to chemotherapy toxicities between the cycles were 11 days in males and 8 days in females. In this study, the recurrence was 32% during the median follow-up of 34 months. Other studies reported recurrence rate from 12-30% [8, 11, 12].

We observed in this study that the median DFS and OS were 57 and 71 months respectively. Five years DFS and OS were 42.8% and 67% respectively. This survival data was not in concordance with the other studies probably because most of our patients were in advanced stage, poor risk groups, and of unfavourable histology. If alone the 5-year survival was seen for all stages excluding stage IV, the survival was good and comparable to other studies indicating the effectiveness of platinum based systemic chemotherapy that was given to all patients. This study highlights that most of the patients presenting to a tertiary care center are in advanced stage with high nodal burden disease. All this ultimately leads to the suboptimal response and suboptimal survival in patients of GCT. However, those who presented in early stage, with favourable histology and underwent multidisciplinary cancer care enjoyed a good long survival.

### Conclusion

GCTs are most frequently diagnosed in adolescence and young patients. If diagnosed earlier, a well-orchestrated multidisciplinary management



approach improves the outcome and survival. In developing countries most of the cases of GCT presents at advanced stage with high nodal burden. It must be emphasised that the GCT is primarily a disease of young and adolescents, therefore these groups of patients should undergo proper investigations and referral, if any suspicion of malignancy is encountered.

### Ethical Approval

The Institutional Research Committee (IRC) at the All India Institute of Medical Sciences, Patna has approved the study (Ref No. AIIMS/Pat/IRC/2020/591, dated 3/11/2020).

### Data Availability

The data sets used or analysed during the current study are available from the corresponding author on reasonable request.

### Conflicts of Interest

None.

### Funding

None.

### Author Contributions

Study concept: Dr. PS; study design: Dr. DS, Dr. JKP, Dr. BK; data acquisition: Dr. DS, Dr. AM; data analysis: Dr. DS; data interpretation: Dr. DS; manuscript preparation: all authors; manuscript review: all authors.

### Abbreviations

**AJCC:** American Joint Committee on Cancer

**AFP:** Alpha-Fetoprotein

**BEP:** Bleomycin, Etoposide, Cisplatin

**βHCG:** Beta Subunit of Human Chorionic Gonadotropin

**CBC:** Complete Blood Count

**CTCAE:** Common Terminology Criteria for Adverse Events

**CECT:** Contrast-Enhanced Computed Tomography

**CI:** Confidence Interval

**DFS:** Disease-Free Survival

**ECOG PS:** Eastern Cooperative Oncology Group Performance Status

**EUROCARE:** European Cancer Registry Based Study on Survival and Care of Cancer Patients

**EP:** Etoposide, Cisplatin

**GCT:** Germ Cell Tumor

**IGCCCG:** International Germ Cell Cancer Collaborative Group

**IHC:** Immunohistochemistry

**KFT:** Kidney Function Test

**LDH:** Lactate Dehydrogenase

**LFT:** Liver Function Test

**MRI:** Magnetic Resonance Imaging

**NACT:** Neoadjuvant Chemotherapy

**NST:** Non Seminomatous

**OS:** Overall Survival

**PFT:** Pulmonary Function Test

**ST:** Seminomatous

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