International Journal of Reproduction, Contraception, Obstetrics and Gynecology
Sangeetha K et al. Int J Reprod Contracept Obstet Gynecol. 2025 Feb;14(2):502-511
www.ijrcog.org
pISSN 2320-1770 | eISSN 2320-1789

DOI: https://dx.doi.org/10.18203/2320-1770.ijrcog20250184

Original Research Article

A study of 44 cases of pure dysgerminoma of the ovary: a single institutional experience

Sangeetha K.*, Ajay Kumar

Department of Obstetrics and Gynecology, Srinivas Medical College and Research Center, Mukka, Mangalore, Karnataka, India

Received: 27 November 2024
Accepted: 03 January 2025

***Correspondence:**
Dr. Sangeetha K.,
E-mail: sangeethamin@gmail.com

ABSTRACT

Background: The extent of surgery and additional therapy required in patients with dysgerminoma is debated. This study evaluated the clinicopathologic characteristics, treatment modalities, long-term survival, and menstrual and fertility outcomes of women with ovarian dysgerminoma managed at our institute.
Methods: A total 44 histologically proven pure ovarian dysgerminoma cases were identified in this retrospective study. Patients who received treatment between 2006 and 2017 at Gujarat Cancer and Research Institute, either surgery or chemotherapy, or both were included.
Results: About 60.6% of patients presented with stage I, 9.09% with stage II, 27.27% with stage III, and 3.03% with stage IV disease. Initial management was surgery followed by observation in 9 (20.45%), surgery followed by adjuvant chemotherapy in 25 (56.81%), and neoadjuvant chemotherapy (NACT) followed by interval debulking surgery (IDS) and adjuvant chemotherapy in 9 (20.45%) patients. Recurrence occurred in 1 (2.32%) patient with stage III disease after 1 year and 5 months (17 months) post-chemotherapy successfully salvaged with platinum-containing chemotherapy. The 3-year disease-free survival (DFS) and overall survival (OS) were 93.18% and 95.45%, respectively. Thirteen patients attempted conception and 6 (46.15%) delivered after treatment completion. Thirty-five patients underwent fertility-sparing surgery. Out of these, thirty patients (85.7%) got regular menstrual cycles. All three prepubertal girls attained menarche.
Conclusions: Regardless of the stage, fertility-sparing surgery can be offered to the patient with good reproductive outcomes expected after fertility-sparing surgery followed by chemotherapy. Adjuvant chemotherapy is associated with significant improvement in DFS. NACT followed by surgery is a reasonable option for patients with advanced-stage dysgerminoma.

Keywords: Pure dysgerminoma, Malignant germ cell tumors, Neoadjuvant chemotherapy, Fertility-sparing surgery

INTRODUCTION

Dysgerminoma is the most common germ cell malignancy, accounting for 1% to 2% of primary ovarian neoplasms and 3% to 5% of ovarian malignancies. Dysgerminoma has been detected in 7-month-old infants to 70 years of age; 7% of dysgerminoma is found in patients younger than 10 years, and 34% are found between age group 10 to 19 years. The average age at diagnosis is 22 years. They also present at a relatively early (stage IA - 65-75%).

Dysgerminoma is composed of germ cells that have not differentiated into embryonic or extraembryonic structures. The stroma is almost always infiltrated with lymphocytes and often contains granuloma similar to those in sarcoidosis. A pure dysgerminoma is endocrinologically inactive. A sign of pronounced hormonal activity indicates the presence of a functioning component, placing the tumor into a mixed germ cell category. A minimally elevated beta human chorionic gonadotropin (HCG) may herald the existence of a

dysgerminoma variant with syncytiotrophoblast cells. Among the different histologic types of ovary germ cell tumors, dysgerminoma showed more serum lactic dehydrogenase (LDH) elevation. There have been several reports which suggest the role of LDH as a tumor marker for dysgerminoma.[1]

Because 85% of all patients with dysgerminomas are younger than 30 years, conservative surgery and preservation of fertility are recommended for those desiring fertility preservation, regardless of the stage.[2] In patients with unilateral salpingo-oophorectomy (USO), careful inspection of the contralateral ovary and exploration to rule out disseminated disease are mandatory. Assessment of the retroperitoneal lymph nodes is an important part of the initial surgery because these neoplasms tend to spread to the lymph nodes, particularly to the high para-aortic nodes. Complete surgical staging (CSS) includes USO, omentectomy, peritoneal biopsies, washings, and bilateral pelvic and para-aortic lymphadenectomy.

Surgery for children or adolescents may differ from that of adult women. Comprehensive staging may be omitted in pediatric patients with early-stage germ cell tumors. Pediatric surgical staging (PSS) was defined as the visual inspection surgical staging, described by Billmire et al, which includes complete resection of the tumor-containing ovary with sparing of the fallopian tube, inspection and palpation of the contralateral ovary, omentum, peritoneal surfaces, and lymph nodes, and collection of peritoneal washings or ascites.[3]

In incompletely staged patients with presumed stage IA disease, the National Comprehensive Cancer Network (NCCN) guidelines suggest checking tumor markers and computed tomography (CT) scanning of the chest, abdomen, and pelvis. If the results are normal, patients may be observed. If any abnormalities are noted laparotomy and complete surgical staging should be performed.

If patients have had incomplete surgical staging, recommended options depend on the type of tumors, the results of imaging and tumor marker testing, the age of the patient, and whether the patient desires fertility preservation. Patients who choose fertility-sparing surgery should be monitored by ultrasound examinations if necessary; completion surgery (category 2B) should be considered after finishing childbearing.

Dysgerminomas are highly sensitive to platinum-based chemotherapy, and treatment can be curative. This fact, coupled with the poor outcomes from surgery alone (even for stage 1 disease), has led to routine administration of adjuvant cisplatin-based chemotherapy to most adult patients except those with stage 1A dysgerminoma. Although 10-15% of stage IA tumors may recur, essentially all of them are salvaged with chemotherapy.[4] The prognosis and clinical features of ovarian dysgerminomas vary by tumor stage, with a five-year survival rate exceeding 75% overall and up to 90% for stage I, though this falls to around 63% for advanced disease. Most cases are diagnosed early, responding well to fertility-sparing surgery, and localized dysgerminomas have a low risk of recurrence or metastasis.[5]

Patients require close follow-up, as 90% of recurrences occur within two years of initial treatment. Most recurrences are treatable with salvage options like surgery, chemotherapy, and occasionally radiation.[2] Recurrences should be treated aggressively with re-exploration and cytoreductive surgery. The excised tissue should be thoroughly examined for signs of germ cell components other than dysgerminoma. Some suspected recurrent dysgerminomas may be mixed germ cell tumors and should be managed appropriately.

The aim of this study is to evaluate clinicopathologic characteristics, treatment modalities, long-term survival, and menstrual and fertility outcomes of women with ovarian dysgerminoma managed at our institution - Gujarat Cancer and Research Institute (GCRI), Ahmedabad.

METHODS

This is a retrospective study in which the medical records of histologically proven pure ovarian dysgerminoma cases were identified. Approval was granted by the institutional review board. Forty-four patients who had received treatment between 2006 and 2017 at Gujarat Cancer and Research Institute, in either surgery or chemotherapy, or both, and who had regular follow-ups, were included in this study. Out of these, 11 patients were operated on outside, and among these, 9 patients received adjuvant chemotherapy at our institute, one patient was kept under observation, and one patient underwent completion surgery at GCRI. A total of 10 patients presented with an advanced stage of disease and ultrasonography (USG)-guided biopsy was suggestive of dysgerminoma and immunohistochemical (IHC) study further confirmed them as pure dysgerminoma. These patients had only raised serum LDH levels and other germ cell markers like serum b-hCG and alpha-fetoprotein (AFP) levels were in normal range. These patients received neoadjuvant chemotherapy (NACT). Among them, only 9 patients had completed treatment (NACT followed by interval debulking surgery (IDS) followed by adjuvant chemotherapy). One patient succumbed during NACT due to tumor lysis syndrome. Twenty-three patients underwent staging laparotomy, and one had completed surgery at our institute.

The clinical data about patient age, menstrual history, obstetric outcomes, symptoms, signs, serum markers, radiology features, type of surgery, intraoperative findings, pre/postoperative treatment, menstrual fertility outcome, and long-term survival were collected. Data about menstrual and fertility outcomes of 4 patients who

were lost to follow-up were obtained by telephone interview.

Patients were staged using the International Federation of Gynecology and Obstetrics (FIGO) staging system. All pathology specimens were reviewed by an expert onco-pathologist at our institute. Patients with advanced stages were given NACT before surgery. The patients who underwent incomplete surgery outside with apparent stage IA were given the option of staging laparotomy or adjuvant chemotherapy. Three patients opted for chemotherapy over restaging surgery. The remaining patients, who underwent staging laparotomy/completion surgery at GCRI, received post-operative adjuvant chemotherapy if they had advanced stage or high-risk early stage.

The patients were followed up till November 2020. The site and characteristics of the relapse, along with the treatment provided, were also documented. Mean overall and disease-free survival (DFS) were calculated.

RESULTS

Patient characteristics

Table 1 provides a summary of the clinical characteristics of the patients. The age at diagnosis ranged from 11 to 48 years. The majority occurred in the 11-15-year-old age group. Four patients had not attained menarche. Among these, 3 patients were aged below 14 years and one patient aged 42 years had primary amenorrhea. One patient with primary amenorrhea had no breast development (karyotyping showed the presence of Y chromosome) and all other premenarcheal girls had thelarche (Tanner stage 1) and secondary sexual characteristics except one patient who was 11 years old. Out of the remaining 40 patients, 39 had regular cycles. Twenty-two patients were unmarried girls. Thirty-two were desirous of future pregnancy.

The most common presenting symptom was a combination of abdominal pain, mass, and distension in 23 patients (52.27%), followed by abdominal mass only in 12 (27.27%), abdominal pain only in 4 (9.09%) and acute abdomen in 2 (4.54%) patients. Infertility, dysuria, and abdominal mass with dry cough were presenting complaints in one patient each (2.27%). The patient who presented with dry cough had pleural effusion on further evaluation. On per abdominal examination, 18 patients (40.90%) had mobile mass, 8 (18.18%) had mass with restricted mobility, 6 (13.63%) had fixed mass, 2 (4.54%) had ascites along with large tumor and 1 patient (2.27%) had nodular mass felt in the left lumbar region. On per vaginal/rectal examination, 6 (13.63%) patients had fixed pelvic mass and the remaining had higher up mass with a smooth pouch of Douglas.

Tumor characteristics

The characteristics of the tumor are shown in Table 2. Preoperative imaging was available in 43 patients, except for one patient operated outside. Tumor size varied from 3 cm to 35 cm. Twenty patients (45.45%) had right-sided tumors and the remaining 24 patients (54.54%) had left-sided tumors. None of the patients had bilateral tumor radiologically. Tumors had radiologic characteristics, like heterogenous echotexture, mixed echogenicity, solid cystic mass, and solid hypoechoic heterogenous lesion with internal necrosis and calcification. One outside incompletely operated patient had multiple peritoneal deposits over the bilateral iliac fossa and umbilical region. Ascites was present in 10 patients (22.72%), and bilateral and unilateral pleural effusion was present in one patient each. Unilateral hydroureteronephrosis (HUN) was noted in 5 patients (83.33%) and bilateral HUN was noted in one patient.

One patient had omental, peritoneal, and mesocolon infiltration. Three patients had mass abutting recto-sigmoid, ureter, and iliac vessels with loss of fat planes. Seven patients had para-aortic node enlargement and two had only iliac node enlargement. One patient had a tumor involving the iliac vessel and psoas muscle. Two patients presented with acute abdomen and had radiological features suggestive of torsion i.e., absence of vascular flow.

Tumor markers, like cancer antigen 125 (CA125) was of range 5-1135 U/ml, AFP 0.5-231 ng/ml, b-hCG 0.1-398 mIU/ml, LDH 170-21350 U/L. One patient had AFP level >231 ng/ml, and five patients had b-hCG levels of more than 100 mIU/ml. All these six patients underwent staging laparotomy at our institute and histopathology and IHC studies were suggestive of pure dysgerminoma. X-ray chest showed pleural effusion in two patients. USG-guided biopsy from adnexal mass or metastatic deposits was done in 17 patients and reports were suggestive of dysgerminoma (n=10), non-Hodgkin lymphoma (NHL) (n=1), poorly differentiated tumor (n=1), epithelial carcinoma (n=1), malignant germ cell tumors (n=4), and IHC confirmation was done in 9 patients. IHC markers like CD117, placental alkaline phosphatase (PLAP), Octamer-binding transcription factor (OCT) ¾, AFP, hCG, and CD30 were used. Ascitic fluid cytology was done in 4 patients and all reports were negative. Pleural fluid cytology was done in 2 patients out of which one patient had malignant effusion.

Treatment characteristics

Table 3 shows the type of treatment modalities received by the patient. Eleven patients were referred from outside the hospital to GCRI after incomplete surgery, on receiving histopathology report suggestive of germ cell tumor/dysgerminoma. Among these, nine patients received adjuvant chemotherapy, one underwent completion surgery, and another patient was kept under observation. Thirty-three patients underwent surgery at GCRI. Among these, nine patients underwent IDS, twenty-three patients underwent staging laparotomy, and one patient had completion surgery.

Table 1: Patient characteristics.

Characteristics	Number (n=44)	Percentage (%)
Age in years		
11-15	14	31.81
16-20	12	27.27
21-25	6	13.63
26-30	6	13.63
>31	6	13.63
Mean	22.47	
Range	11-48	
Menstrual history		
Not attained menarche	4	9.09
Attained	40	90.90
Regular cycles	39	97.5
Irregular cycles	1	2.5
Secondary sexual characteristics		
Developed	42	95.45
Not developed	2	4.54
Marital history		
Married	22	50
Unmarried	22	50
Desirous of pregnancy	32	72.72
Family completed	12	27.27
Presenting complaints		
Abdominal pain, mass, distension	23	52.27
Abdominal mass only	12	27.27
Abdominal pain only	4	9.09
Acute abdomen	2	4.54
Infertility	1	2.27
Dysuria	1	2.27
Abdominal mass with dry cough	1	2.27
Per abdominal examination		
Firm mobile mass	18	40.90
Restricted mobility	8	18.18
Fixed mass	6	13.63
Ascites	2	4.54
Unbooked case	8	18.18
No palpable mass	1	2.27
Nodular mass at left lumbar region	1	2.27

Table 4 shows the type of surgeries offered to the patients. Eleven patients underwent incomplete surgery at outside hospitals. Four patients underwent USO by laparotomy. Two underwent laparoscopic USO. Emergency laparotomy and USO for torsion were done in two patients.

One pregnant lady underwent ovarian mass removal at the time of lower segment caesarean section (LSCS). USO with omental biopsy and USO with contralateral ovarian biopsy was done in one patient each.

Table 2: Preoperative radiological and pathological characteristics of tumor.

Tumor characteristics	Number (n=44)	Percentage (%)
Size of the tumor in cm		
<10	16	36.4
10-19	18	40.9
>20	10	22.7
Range	3-35 cm	
Mean	13.12	
Laterality		
Left	24	54.54
Right	20	45.45
Ascites		
No	34	77.27
Minimum	6	13.63
Moderate	1	2.27
Gross	3	6.81
Ascitic fluid cytology (n=4)		
Positive	Nil	0
Negative	4	100
Plural effusion		
No	42	95.45
Unilateral	1	2.27
Bilateral	1	2.27
Pleural fluid cytology (n=2)		
Positive	1	50
Negative	1	50
Hydroureteronephrosis (n=6)		
Unilateral	5	83.33
Bilateral	1	16.66
CA125 (n=41)		
Normal	15	36.58
Elevated	26	63.41
AFP (n=39)		
Normal	35	89.74
Elevated	4	10.25
b-hCG (n=40)		
Normal	18	45
Elevated	22	55
LDH (n=42)		
<500	10	23.80
500-1000	6	14.28
>1000	26	61.90
USG-guided biopsy (n=17)		
Dysgerminoma	10	58.82
Poorly differentiated tumor/ lymphoma/germ cell tumor	1	5.88
NHL	1	5.88
Epithelial carcinoma	1	5.88
Malignant germ cell tumor	4	23.52
IHC confirmation	9	52.94

A total of 33 patients underwent surgeries at GCRI. Eighteen fertility-sparing and five fertility non-sparing

staging laparotomies were done. Fertility-sparing staging laparotomy consists of wash cytology/ascitic fluid cytology, exploration of the peritoneal cavity, USO, unilateral pelvic lymph node dissection, dissection of suspicious para-aortic nodes, multiple peritoneal biopsies, and omentectomy. Fertility non-sparing surgery includes peritoneal fluid cytology, total abdominal hysterectomy with bilateral salpingo-oophorectomy (TAH+BSO), bilateral pelvic lymph node dissection, infracolic omentectomy, suspicious para-aortic node dissection, and peritoneal biopsies. Ten patients presented with advanced stage of disease and USG-guided biopsy was suggestive of dysgerminoma and IHC study further confirmed them as pure dysgerminoma. These patients had only raised serum LDH levels and other germ cell markers like serum b-hCG and AFP levels were in normal range. These patients received NACT; among them, only 9 patients had completed treatment (NACT followed by IDS and adjuvant CT). One patient succumbed during NACT due to tumor lysis syndrome. Fertility-sparing IDS was done in seven patients and fertility non-sparing IDS in two patients. One outside-operated patient who had undergone ovarian mass removal during LSCS, underwent completion surgery. Four patients had suboptimal surgery (Table 3) – one had 3×4 cm para-aortic node adherent to inferior vena cava, the second patient had 5 cm unresectable tumor in POD and multiple left iliac lymph nodes adherent to vessels, the third patient had mesenteric lesion, and the fourth patient had 5×5 cm lesion over POD infiltrating rectum along with 1 cm disease at the under surface of diaphragm.

The histopathological characteristics are shown in Table 5. Peritoneal cytology was available only in patients who got operated at our institute. Twenty-four cytology reports were available; all being negative for malignant cells. Information regarding capsular status was available in 39 patients. Twenty-one patients had tumors with intact capsules, pre-operative rupture was seen in two patients, intra-operative rupture in four, capsular infiltration by tumor in twelve patients, and capsular status was not known in four patients. Sixteen patients had lympho-vascular stromal invasion. One patient had laparoscopic piecemeal removal of the tumor. One patient had bilateral ovarian involvement. Four patients had metastatic deposits over the bladder peritoneum/mesentery/over infundibulo-pelvic ligament/bowel serosa and POD. One patient had a positive obturator node. Suspicious/enlarged para-aortic nodes were removed in five patients, of which three were harboring malignant cells. All nine patients who had undergone IDS had non-viable tumor at the final histopathological examination (pathological complete response). Table 6 summarizes the stage-wise patient distribution who were operated on at our institute.

Table 7 shows the types of chemotherapy regimens used in these patients. Altogether thirty-four patients received chemotherapy at our institute. Nine patients were kept under observation (one outside-operated patient and eight patients who had complete staging at our institute). Nine patients, who were operated outside, received only adjuvant chemotherapy at our institute. Among these, three patients who had apparent stage IA disease, but who had raised post-operative LDH, had been given the option of staging laparotomy or adjuvant chemotherapy. The patients opted for chemotherapy over restaging surgery. The remaining six patients were given adjuvant chemotherapy since they had advanced-stage or high-risk early-stage disease. One patient, after completion of 3 cycles of adjuvant bleomycin, etoposide, and cisplatin (BEP), had residual disease (enlarged iliac node with inconclusive biopsy report) and raised LDH. So, she received three more cycles of carboplatin and etoposide.

Table 3: Treatment modalities received by patients.

Treatment modality	Number (n=44)	Percentage (%)
Surgery only	9	20.45
Surgery + adjuvant chemotherapy	25	56.81
NACT + surgery+ adjuvant chemotherapy	9	20.45
NACT only (died after one cycle)	1	2.27
Characteristics of surgery (n=43)		
Incomplete surgery outside followed by completion surgery at our institute + no adjuvant chemotherapy	1	2.32
Incomplete surgery outside followed by adjuvant chemotherapy at our institute	9	20.93
Incomplete surgery outside followed by observation at our institute	1	2.32
Staging surgery at GCRI followed by observation	8	18.60
Staging surgery at GCRI followed by adjuvant chemotherapy	15	34.88
Interval debulking at GCRI followed by adjuvant chemotherapy	9	20.93
Outcome of surgery at GCRI (n=33)		
Optimal surgery	29	87.87
Suboptimal surgery	4	12.12

Fifteen patients who had staging laparotomy at GCRI received adjuvant chemotherapy. Two patients with stage IC1 received three cycles of only etoposide and carboplatin as adjuvant chemotherapy. Nine patients with advanced disease took NACT followed by IDS followed by adjuvant chemotherapy. One patient was wrongly diagnosed as epithelial ovarian carcinoma outside and received one cycle of single-agent carboplatin and later, on slide review, was diagnosed as dysgerminoma and

underwent staging laparotomy followed by adjuvant chemotherapy at GCRI.

Table 4: Type of surgeries offered to patients.

At outside hospital	n=11	%
USO by laparotomy	4	36.36
USO by laparoscopy	2	18.18
LSCS with ovarian mass removal	1	9.09
Emergency laparotomy for torsion ovary followed by USO	2	18.18
USO with omental biopsy	1	9.09
USO with contralateral ovarian biopsy	1	9.09
At GCRI (n=33)		
Staging laparotomy (fertility-sparing)	18	54.54
Staging laparotomy (fertility non-sparing)	5	15.15
IDS (fertility-sparing)	7	21.21
IDS (fertility non-sparing)	2	6.06
Completion surgery	1	3.03

Table 5: Histopathological characteristics.

Characteristics	Number	%
Peritoneal cytology (n=24)		
Positive	0	0
Negative	24	100
Capsule status (n=39)		
Intact	21	53.84
Intraoperative rupture	4	10.25
Pre-operative rupture	2	5.12
Capsular infiltration	12	30.76
Status not known	4	10.25
Contralateral ovary involvement	1	2.27
Lymphovascular invasion (n=42)		
Yes	16	38.09
No	26	61.90
Pelvic lymph nodes (n=34)		
Positive	1	2.94
Negative	33	97.05
Para-aortic nodes (n=5)		
Positive	3	60
Negative	2	40
Omentum (n=35)		
Positive	0	0
Negative	35	100
Metastatic deposit	4	9.09

Recurrence and survival outcome

On follow-up, out of 43 patients, only one patient, who had stage III disease at presentation and underwent suboptimal surgery with residual disease at POD and unresectable para-aortic nodes, had elevated LDH level and enlarged para-aortic nodes on imaging. So, she received two cycles of EP chemotherapy and is presently under observation. This patient had DFS of 1 year and 5 months (17 months). The other three patients with suboptimal surgery were disease-free post adjuvant chemotherapy. Two patients (4.54%) died due to chemotherapy adverse effects. With follow-up, the 3-year DFS and overall survival (OS) were 93.18% and 95.45%, respectively.

Table 6: Stage-wise distribution of patients operated at GCRI.

Stage	Number (n=33)	%
IA	8	24.24
IB	1	3.03
IC1	2	6.06
IC2	9	27.27
IC3	0	0
IIA	0	0
IIB	3	9.09
IIIA	5	15.15
IIIB	0	0
IIIC	4	12.12
IVA	1	3.03
IVB	0	0

Table 7: Chemotherapy regimen received at GCRI.

Types of chemotherapy regimens (n=34)	Number	%
NACT (n=10)		
1 cycle single agent carboplatin + 2 cycles of BEP	1	10
2 cycles of BEP	7	70
1 cycle of EP + 2 cycles of BEP	1	10
1 cycle of BEP (patient expired)	1	10
Incomplete surgery outside followed by adjuvant chemotherapy (n=9)		
3 cycles of BEP	3	33.33
4 cycles of BEP	5	55.55
3 cycles of BEP + 3 cycles of EP	1	11.11
Staging surgery at GCRI followed by adjuvant chemotherapy (n=15)		
3 cycles of BEP	10	66.66
4 cycles of BEP	3	20
3 cycles of carboplatin + etoposide	2	13.33

Major chemotherapy complications

One patient who had undergone IDS and received one cycle of adjuvant BEP died due to severe febrile neutropenia after 8 days post chemotherapy. One patient with advanced-stage disease who was receiving the first cycle of BEP as NACT died due to tumor lysis syndrome. Three patients had seroconversion and became hepatitis B surface antigen (HBsAg) positive. One patient developed pulmonary tuberculosis after one-year post-chemotherapy. One patient developed B cell acute lymphoblastic

leukemia (B-ALL) after six years of completion of chemotherapy and is presently on chemotherapy and curative radiotherapy.

Menstrual outcome

In our study, 36 patients underwent fertility-sparing surgery. Out of these, thirty patients (83.33%) have got regular, and one patient (2.77%) has got irregular menstrual cycles. All three prepubertal girls (100%) attained menarche following treatment completion. One patient, who had bilateral dysgerminoma and underwent contralateral ovarian biopsy, developed irregular cycles and became infertile. One patient (2.77%) had secondary amenorrhea for which she took hormonal therapy and is presently having regular cycles. So only three patients (8.33%) following adjuvant chemotherapy developed irregular cycles.

Fertility outcome

In our study, 32 patients were desirous of future pregnancy. Among them, 19 girls are still unmarried. Thirteen patients attempted conception; of these three patients were married for less than one year with no pregnancy till data collection. One infertile patient adopted two children, and the other two infertile patients (15.38%) are on infertility treatment. Six patients (46.15%) delivered after treatment completion. One patient was a known case of abdominal tuberculosis and was on anti-tubercular treatment and she is infertile.

DISCUSSION

Dysgerminomas are the most frequently occurring malignant germ cell tumors, making up roughly 30% to 40% of ovarian cancers originating from germ cells.[6] Dysgerminomas comprise only 1-3% of all ovarian cancers but account for 5-10% of cases in patients under 20 years old.[6] Dysgerminoma consists of germ cells that have not differentiated to form embryonic or extraembryonic structures. Debate has focused on the extent of surgery and additional therapy required to treat this group of patients as randomized data in this patient population are scarce. As this disease carries an excellent prognosis and the age of the majority of patients is less than 30 years (85%), fertility and long-term sequelae of treatment are important factors in considering treatments.

Dysgerminomas primarily occur in young women, with 75% diagnosed between ages 10 and 30, about 5% in those under 10, and rarely in women over 50. Due to their prevalence in younger women, dysgerminomas make up 20% to 30% of ovarian cancers found during pregnancy.[6] In our study, majority of the patients belonged to the age group of 11-20 years (59.09%) with a mean age of diagnosis at 22.47 years. The remaining 12 (27.26%) patients belonged to the age group of 21-30 years and 6 (13.63%) patients were more than 31 years of age. In a study by Viscus et al., the mean age was 22.2 years, which is similar to our study. Bilateral oophorectomy was done in 21.5% of cases and unilateral oophorectomy was done in 72.2% of cases.[7]

Most patients presented with abdominal enlargement, a growing mass or pain. The growth of dysgerminoma is usually rapid. As a result, patients commonly present with abdominal distension and pain caused by rupture leading to hemoperitoneum or torsion. In our study, 52.27% of patients had abdominal pain, mass, or distension at presentation, 27.27% had only abdominal mass, and 9.09% had presented with only abdominal pain as their complaint.

As dysgerminoma occurs more frequently in young patients, extirpation of the disease involves decisions concerning childbearing and probabilities of recurrence. Adjuvant chemotherapy is the standard of care, except for those with stage IA dysgerminoma.[8] Comprehensive staging allows patients to be appropriately risk-stratified and selected for surveillance versus adjuvant therapy. If childbearing has been completed, then BSO and hysterectomy are performed in addition to a full staging procedure.[9] Fertility-sparing surgery (FSS) generally includes conserving the contralateral ovary and the uterus, along with staging surgery.[10] Cytoreductive surgery is of unproven value, but a bulky disease that can be readily resected (e.g., an omental cake) should be removed as an initial operation. In our study, 54.54% of the patients underwent fertility-sparing staging laparotomy and 21.21% of the patients with advanced disease underwent fertility-sparing IDS.

In 28% of cases, dysgerminomas show lymph node metastasis, which is significantly linked to a reduced 5-year survival rate of 82.8%.[11] In our study, 5 patients had enlarged suspicious para-aortic nodes, among which 3 patients had metastatic lymph nodes.

Many patients with a dysgerminoma will have a tumor that is confined to one ovary and will be referred to USO without surgical staging. The options for such patients are: repeat laparotomy for surgical staging, regular pelvis and abdominal CT scan, or adjuvant chemotherapy.[12] The decision to perform another surgery on patients who were not staged during their initial procedure is contentious, as those with recurrences can often be effectively treated with chemotherapy. Incompletely staged patients with presumed stage IA disease**,** National Comprehensive Cancer Network (NCCN) guidelines suggest to check tumor markers and computed tomography (CT) scanning of the chest, abdomen, and pelvis. If results are normal, patients can be observed. If any abnormalities are detected during these tests, laparotomy and comprehensive surgical staging should be conducted. In our study, one outside-operated patient was kept under observation who had fulfilled above mentioned criteria. Three patients with apparent stage IA tumors who had raised LDH were given the option of staging laparotomy or adjuvant

chemotherapy. Those patients opted for adjuvant chemotherapy rather than surgery.

Incompletely staged patients with higher-stage tumors should receive adjuvant treatment. Six outside-operated patients were given adjuvant chemotherapy depending on their intraoperative findings and final histopathology reports (i.e., tumor rupture, and capsular infiltration).

The regimen of choice is BEP.[13] The optimal number of cycles has not been established in randomized trials. NCCN recommends three courses of adjuvant therapy for completely resected stage I disease and four courses for those with more advanced stage disease. Twenty-three patients underwent staging laparotomy at GCRI, and fifteen patients received adjuvant chemotherapy BEP. Ten patients with stage 1C disease took 3 cycles of BEP, one patient with stage II and two patients with stage III disease took 4 cycles of BEP. Two patients with stage IC1 received three cycles of only etoposide and carboplatin as adjuvant chemotherapy as bleomycin was contraindicated.

In patients with widespread disease, NACT may be warranted. Few trials, and certainly no randomized trials, are available to answer the question regarding utility in these patients. Talukdar et al assessed the use of neoadjuvant chemotherapy (NACT) with four cycles of BEP, followed by fertility-sparing surgery, in 23 patients with bulky disease. This was compared to 43 patients who underwent primary debulking surgery for FIGO stage III or IV disease during the same period. After NACT, 21 patients showed a response to treatment with 16 achieving a complete response and 5 with a partial response. Eighteen of 21 patients in the NACT group were then able to undergo fertility-sparing and surgery, and those with residual disease were given an additional two cycles of BEP. Of the evaluable patients, 21 of 23 patients survived with a median DFS period of 211 months.[14] In our study, we included 10 patients with advanced-stage, biopsy-proven, IHC-confirmed dysgerminoma, who had only raised serum LDH level (other germ cell markers being in the normal range) and received BEP as NACT (9 patients underwent IDS following completion of NACT and 1 patient died after the first cycle of NACT). Among these 9 patients, 7 patients underwent fertility-sparing, and 2 patients underwent fertility non-sparing surgery. All had optimal debulking surgery. All patients had non-viable tumors at histopathological examination (pathological complete response), and they received adjuvant BEP chemotherapy.

The development of secondary tumors is a significant cause of late morbidity and mortality in patients undergoing chemotherapy for germ cell tumors. Specifically, etoposide has been linked to the occurrence of treatment-related leukemias. The chance of developing treatment-related leukemia following etoposide is dose-related. The incidence of leukemia is approximately 0.4-0.5% (representing a 30-fold increased likelihood) in patients receiving a cumulative etoposide dose of less than 2,000 mg/m^2 compared with as much as 5% (representing a 336-fold increased likelihood) in those receiving more than 2,000 mg/m^2. In a typical three- or four-cycle course of BEP, patients receive a cumulative etoposide dose of 1,500 or 2,000 mg/m^2, respectively.[15] Despite the risk of secondary leukemia, risk-benefit analyses concluded that etoposide-containing chemotherapy regimens are beneficial in advanced germ cell tumors. In our study, one patient developed B-ALL after six years post-chemotherapy.

Although temporary ovarian dysfunction or failure is common with platinum-based chemotherapy, most women will resume normal ovarian function, and childbearing is usually preserved. In a representative study involving 47 patients treated with combination chemotherapy for germ cell malignancies, 91.5% of the patients regained normal menstrual function, resulting in 14 healthy live births without any reported birth defects.[16]

In our study, 36 patients underwent fertility-sparing surgery. Out of these, thirty patients (83.33%) have got regular, and one patient (2.77%) has got irregular menstrual cycles. All three prepubertal girls (100%) attained menarche following treatment completion. Only three patients (8.33%) following adjuvant chemotherapy developed irregular cycles. In a study by Yoo et al, of the nine premenarchal patients, eight (88.9%) subsequently had normal menarche. Among the 16 adolescent patients, 15 (93.8%) resumed normal menstruation and 1 had premature ovarian failure.[17] Brewer et al, observed that 71% of young women who were treated with BEP after fertility-sparing surgery for pure dysgerminoma maintained their normal menstrual function during and after chemotherapy.[18]

In this study, 32 patients were desirous of future pregnancy. Thirteen patients attempted conception, of which three patients were married for less than one year with no pregnancy till data collection. Six patients (46.15%) delivered after treatment completion. At the end of treatment, 4 patients (30.76%) were infertile. In a study by Anita et al, after treatment, 71.4% resumed their menstrual cycles within 6 months.[19] In another study by Husaini et al, sixteen (32%) patients attempted conception, 14 of whom had healthy infants without congenital defects.[20]

In our study, with follow-up, the 3-year DFS and OS were 93.18% and 95.45%, respectively. In the study by Husaini et al, 5-DFS and OS were 88% (95% confidence interval (CI), 78.2–97.8%) and 95.2% (95% CI, 89.3–100%), respectively.[20] In a study by Kdous et al, which included only dysgerminoma cases, the 5-year survival rate was 91.7%.[21]

Survival of patients with stage I disease was 98.2% and that for patients with advanced disease stages was 94.4%, as seen in a study by Low et al.[16] In our study, the 5-year DFS and OS were 93.18% and 95.45%, respectively. The

recurrence in our study occurred at 1 year 5 months (17 months), similar to 12 months previously reported by Patterson et al.[8]

CONCLUSION

Most patients with dysgerminoma are diagnosed with stage I disease. Complete surgical staging is required for diagnosis, staging, and treatment. However, the potential benefits and risks of aggressive cytoreductive surgeries for advanced disease need to be carefully evaluated for these tumors, which are particularly sensitive to chemotherapy. Fertility-preserving surgery can be done safely with favourable outcome regardless of stage. These patients can be treated with USO and can be observed carefully with regular pelvic examinations, abdominopelvic CT, and tumor markers, including LDH. Adjuvant chemotherapy is the standard of care, except for those with stage IA dysgerminoma. The majority of patients receive three cycles of BEP chemotherapy. Favourable reproductive outcomes can be expected after fertility-sparing surgery followed by chemotherapy. Adjuvant chemotherapy was linked to a marked improvement in disease-free survival (DFS). NACT followed by surgery is a reasonable option for patients with advanced-stage dysgerminoma.

ACKNOWLEDGEMENTS

The authors would like to thank the patients and families involved in this study and the medical and nursing staff at the Gujarat Cancer and Research Institute, Ahmedabad, for their support in data collection and patient care. They would also like to acknowledge the oncology pathology team and the technical assistance from the research staff.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Friedman M, White RG, Nissenbaum MM, Browde S. Serum lactic dehydrogenase-A possible tumor marker for an ovarian dysgerminoma: A literature review and a report of a case. Obstet Gynecol Surv. 1984;39:247-51.
2. Beffa LB, Sung CJ, DiSilvestro PA. Germ cell, stromal, and other ovarian tumors. In: Creasman WT, Mutch DG, Mannel RS, Tewari KS, editors. DiSaia and Creasman Clinical Gynecologic Oncology. 10th edition. Elsevier. 2023;282-310.e7.
3. Billmire D, Vinocur C, Rescorla F, Cushing B, London W, Schlatter M, et al; Children's Oncology Group (COG). Outcome and staging evaluation in malignant germ cell tumors of the ovary in children and adolescents: an intergroup study. J Pediatr Surg. 2004;39(3):424-9.
4. Michener CM. Ovarian Dysgerminomas Treatment & Management. In: Randall LM, editor. Drugs & Diseases Obstetrics & Gynecology. 2024. Medscape. Available at: https://emedicine.medscape.com/article/253701-treatment. Accessed on 25 October 2024.
5. Tîrnovanu MC, Florea ID, Tănase A, Toma BF, Cojocaru E, Ungureanu C, et al. Uncommon Metastasis of Ovarian Dysgerminoma: A Case Report and Review of the Literature. Medicina (Kaunas). 2021;57(6):534.
6. Berek JS, Bast RC Jr. Nonepithelial Ovarian Cancer. In: Kufe DW, Pollock RE, Weichselbaum RR, editors. Holland-Frei Cancer Medicine. 6th edition. Hamilton (ON): BC Decker. 2003.
7. Vicus D, Beiner ME, Klachook S, Le LW, Laframboise S, Mackay H. Pure dysgerminoma of the ovary 35 years on: a single institutional experience. Gynecol Oncol. 2010;117(1):23-6.
8. Patterson DM, Murugaesu N, Holden L, Seckl MJ, Rustin GJ. A review of the close surveillance policy for stage I female germ cell tumors of the ovary and other sites. Int J Gynecol Cancer. 2008;18(1):43-50.
9. Seppälä TT, Dominguez-Valentin M, Crosbie EJ, Engel C, Aretz S, Macrae F, et al. Uptake of hysterectomy and bilateral salpingo-oophorectomy in carriers of pathogenic mismatch repair variants: a Prospective Lynch Syndrome Database report. Eur J Cancer. 2021;148:124-33.
10. Canlorbe G, Chabbert-Buffet N, Uzan C. Fertility-Sparing Surgery for Ovarian Cancer. J Clin Med. 2021;10(18):4235.
11. Hyseni N, Llullaku S, Jashari H, Zahiti K, Hyseni F, Kurshumliu F, et al. Advanced ovarian dysgerminoma infiltrating both ovaries and uterus in a 7-year-old girl. Case Rep Oncol Med. 2014;2014:910852.
12. Lu KH, Gershenson DM. Update on the management of ovarian germ cell tumors. J Reprod Med. 2005;50(6):417-25.
13. Rogers PC, Olson TA, Cullen JW, Billmire DF, Marina N, Rescorla F, et al; Pediatric Oncology Group 9048; Children's Cancer Group 8891. Treatment of children and adolescents with stage II testicular and stages I and II ovarian malignant germ cell tumors: A Pediatric Intergroup Study--Pediatric Oncology Group 9048 and Children's Cancer Group 8891. J Clin Oncol. 2004;22(17):3563-9.
14. Talukdar S, Kumar S, Bhatla N, Mathur S, Thulkar S, Kumar L. Neo-adjuvant chemotherapy in the treatment of advanced malignant germ cell tumors of ovary. Gynecol Oncol. 2014;132(1):28-32.
15. Kollmannsberger C, Beyer J, Droz JP, Harstrick A, Hartmann JT, Biron P, et al. Secondary leukemia following high cumulative doses of etoposide in patients treated for advanced germ cell tumors. J Clin Oncol. 1998;16(10):3386-91.
16. Low JJ, Perrin LC, Crandon AJ, Hacker NF. Conservative surgery to preserve ovarian function in patients with malignant ovarian germ cell tumors. A review of 74 cases. Cancer. 2000;89(2):391-8.
17. Yoo SC, Kim WY, Yoon JH, Chang SJ, Chang KH, Ryu HS. Young girls with malignant ovarian germ cell tumors can undergo normal menarche and

menstruation after fertility-preserving surgery and adjuvant chemotherapy. Acta Obstet Gynecol Scand. 2010;89(1):126-30.
18. Brewer M, Gershenson DM, Herzog CE, Mitchell MF, Silva EG, Wharton JT. Outcome and reproductive function after chemotherapy for ovarian dysgerminoma. J Clin Oncol. 1999;17(9):2670.
19. Anita AN, Rushdan MN. Reproductive function after treatment of ovarian germ cell malignancy. Med J Malaysia. 2012;67:71-6.
20. Al Husaini H, Soudy H, El Din Darwish A, Ahmed M, Eltigani A, Al Mubarak M, et al. Pure dysgerminoma of the ovary: a single institutional experience of 65 patients. Med Oncol. 2012;29(4):2944-8.
21. Kdous M, Hachicha R, Gamoudi A, Boussen H, Benna F, Rahal K. Pure dysgerminoma of the ovary. 12 case reports. Tunis Med. 2003;81(12):937-43.

Cite this article as: Sangeetha K, Kumar A. A study of 44 cases of pure dysgerminoma of the ovary: a single institutional experience. Int J Reprod Contracept Obstet Gynecol 2025;14:502-11.