

## Management of ovarian cancer a retrospective study and review of literature.

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### Abstract

**Introduction:** Epithelial ovarian cancer is the most lethal gynecological malignancy diagnosed at an advanced stage in the majority of the cases. Management includes primary debulking surgery followed by paclitaxel and carboplatin-based chemotherapy. Neoadjuvant chemotherapy (NACT) followed by interval debulking surgery (IDS) is an alternative option in selected cases of advanced disease. Germ cell malignancies occur in younger age with a good prognosis.

**Material and Methodology:** A retrospective study of cases visiting our unit for treatment in year 2023-2024 were performed to see the outcomes as we mature to perform more optimal surgery. Altogether 95 cases of carcinoma ovary who had optimally written case notes for retrieval of information for analysis were taken for study and analyzed.

**Results:** Out of 95 cases, 72 cases (75.78%) were epithelial ovarian malignancies, 18 (18.94%) were germ cell tumors, and 5(5.26%) were borderline tumors. Among epithelial ovarian malignancies high-grade serous carcinoma was the commonest histologic type, mucinous borderline tumors were common among borderline tumors and yolk sac tumors were common among germ cell malignancies. The majority of cases of epithelial ovarian cancer 28 (38.9%) were in the age group of 40-50 years and 75% of them were in advanced stages III and IV. The majority of cases, 33 (45.8%) underwent NACT followed by IDS, 24 (33.3%) underwent primary debulking surgery, and 15 cases (20.8%) received only palliative chemotherapy. The majority of cases of germ cell malignancies were managed by fertility-sparing surgery followed by adjuvant chemotherapy.

**Conclusions:** Epithelial ovarian cancer is a lethal gynecological malignancy. Primary debulking surgery followed by platinum-based chemotherapy is the standard treatment. Borderline ovarian tumors are common in women of reproductive age 30-40s whereas germ cell malignancies are common in younger girls below 20 years.

**Keywords:** Borderline ovarian tumors, Epithelial Ovarian Cancer, Germ cell malignancies, Interval Debulking Surgery, Neoadjuvant Chemotherapy

### Introduction

Ovarian cancer is the most lethal gynecological cancer<sup>1</sup>. In Nepal, it is the second most common gynecological cancer after cervical cancer<sup>2</sup>. Among malignant ovarian neoplasms, more than 90% of cases are epithelial ovarian cancer. The

majority of cases present at an advanced stage with a low 5-year survival rate of less than 50%<sup>3</sup>. Primary debulking surgery (PDS) followed by platinum-based adjuvant chemotherapy is the standard treatment. Interval debulking surgery

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after neoadjuvant chemotherapy followed by adjuvant chemotherapy is an option in selected cases.<sup>4</sup> Even after a complete clinical response recurrence is seen at a higher rate leading to death due to disease<sup>5</sup>. Germ cell tumors predominate in younger ages below 20, while borderline tumors typically occur in women in their 30s and 40s— 10 or more years younger than in women with invasive epithelial ovarian cancer<sup>6</sup>. Various issues are emerging regarding managing ovarian cancer so the present study gives an overview of our management with highlights from the literature review where we can improve.

### Materials and methods

A retrospective study was conducted taking case notes of carcinoma ovary patients visiting gynecology oncology unit of B. P. Koirala Memorial Cancer Hospital, Chitwan during the period of year 2023 and 2024. Ethical approval was taken from the Institutional Review Committee of BPKMCH. Total of 95 case notes were retrieved and deemed complete for analysis. A set of fixed Proforma-based questionnaires were designed, and the retrieved information were filled from the case notes. Statistical analysis was performed using SPSS 25.

### Results

Out of 95 cases, 72 (75.78%) cases were epithelial ovarian malignancies, 18 (18.94%) were germ cell tumors, and 5 (5.26%) were borderline tumors. Out of 72 cases of epithelial ovarian malignancy, the majority of cases 28 (38.9%) were in the age group of 40-50 years as shown in Table 1. The age group ranges from 30 to 75 years with a mean of 50.63 and SD of 10.78.

The majority of cases, 33 (45.8%) underwent NACT followed by IDS, 24 (33.3%) underwent primary debulking surgery, and 15 cases (20.8%) received only palliative chemotherapy only. The

majority of cases were in stage IIIC 20 (27.8%) cases, followed by stage IVB 17 (23.6%) cases, IIIB 9 (12.5%) cases as shown in the table below.

Table 1: Age of the ovarian cancer patients

Age group (years)	Number (n)	Percent (%)
30-40	9	12.5
41-50	28	38.9
51-60	23	31.9
61-70	9	12.5
71-80	3	4.2
	Total (72)	

Regarding the operative procedures carried, out of 57 cases who underwent surgery, the majority of cases 47 (65.3%) underwent TAH with BSO with omentectomy with the addition of appendectomy in 6 cases (8.3%), cholecystectomy was added to the above procedure in 2 cases (2.8%), limited bowel resection was done in 1 case (1.4%), 1 case had only TAH with BSO.

Table 2: Staging of the ovarian cancer patients

STAGE (FIGO 2009)	Number (n)	Percent (%)
Stage IA	6	8.3
Stage IB	4	5.6
Stage IC	5	6.9
Stage II	3	4.2
Stage IIIA	5	6.9
Stage IIIB	9	12.5
Stage IIIC	20	27.8
Stage IVA	3	4.2
Stage IVB	17	23.6
	Total (72)	

At histology, Majority of cases 45 (62.5%) out of 57 had high-grade serous carcinoma, 7 cases (9.7%) had mucinous carcinoma, and 4 cases (5.6%) had low-grade serous carcinoma. And one case had endometrioid carcinoma.

Recurrence was documented in 31 cases (43.1%) out of 57 cases who underwent surgery. Most recurrences were in the pelvis 13(18%), retroperitoneal nodes in 9 cases (12.5%), peritoneum 5 (6.1%) liver in 4 cases (5.6%)

5 cases of borderline tumors had an age range between 20-62 years with a mean age of 46 years. Four cases were of mucinous borderline tumors, and one case was of serous borderline tumors.

**Table 3: Age distribution of GCT**

Age group (years)	Number (n)	Percent (%)
10-20	9	50
21-30	6	33.33
31-40	2	11.11
41-50	1	5.55

Histological types of germ cell tumors and their management are shown in the table below:

**Table 4: Histological types of GCT**

Histological Type	Number of cases	Management
Yolk sac tumor	5	FSS followed by ACT
Immature teratoma	5	FSS followed by ACT
Dysgerminoma	3	FSS followed by ACT
Squamous cell carcinoma arising in mature cystic teratoma	1	Case1-TAH with LSO With appendectomy with omentectomy following RSO
	1	Case 2- TAH with BSO followed by ACT
	1	Case 3_ TAH with BSO With appendectomy with omentectomy with resection of sigmoid colon with bladder repair
Mixed germ cell tumor	2	FSS followed by ACT

Young patients with the age of 20 or less were encouraged to undergo Fertility sparing surgery (FSS) when they had tumors. Majority of them had salpingo-oophorectomy. Two patients had

TAH with BSO, 3 cases were only diagnosed after unilateral salpingo-oophorectomy underwent completion surgery later in the course as they have completed the family.

In germ cell tumors, 18 cases were there in this cohort. The age range was between 11-50 years, with a mean age of 22.72 with SD 10.60.

## Discussion

Epithelial ovarian cancer is seen at an advanced stage in most cases. Primary debulking surgery (PDS) with a target of complete tumor resection followed by carboplatin plus paclitaxel is the standard treatment for ovarian cancer. If the disease is advanced with unresectable sites involved so that the target of complete resection of the tumor cannot be achieved or if due to severe comorbidities patient cannot undergo extensive upfront surgery, then the alternative treatment is neoadjuvant chemotherapy followed by interval debulking surgery (IDS) or palliative treatment<sup>7</sup>. In the present study also majority of cases 75 % were in advanced stages III and IV.

A Randomized Trial of Lymphadenectomy in Patients with Advanced Ovarian Neoplasms (LION Trial ) showed no benefit of systematic lymphadenectomy in terms of overall or progression-free survival in patients with advanced ovarian cancer who had undergone macroscopically complete tumor resection and had normal lymph nodes both before and during surgery but was associated with a higher incidence of postoperative complications<sup>8</sup>. Complete tumor resection at upfront surgery is the most important prognostic factor for patients with advanced ovarian cancer (AOC).

Bevacizumab, in combination with platinum-based chemotherapy, followed by bevacizumab alone as maintenance, has been approved by the FDA for treatment of patients with advanced EOCs after initial surgical intervention, following the results of the GOG-0218 and ICON-7 studies<sup>9</sup>. The use of PARP inhibitors (PARPi) in patients with epithelial ovarian cancer is expanding, initially it was used in recurrent

disease but now it is also used in the first-line setting<sup>10</sup>. In 2017, the olaparib monotherapy was approved by the FDA for maintenance treatment for platinum-sensitive, relapsed ovarian cancers regardless of the presence or absence of BRCA mutations. Based on the objective evidence from the SOLO-1 trial, the FDA approved the olaparib monotherapy as the first-line maintenance treatment for patients with platinum-sensitive advanced (FIGO stage III–IV), high-grade, BRCA-associated ovarian cancers in 2018. The FDA approval for olaparib plus bevacizumab as maintenance therapy for patients with newly diagnosed, advanced, high-grade ovarian cancers who have responded to first-line platinum-based chemotherapy plus bevacizumab is supported by the results of the PAOLA-1 trial (2019)<sup>9</sup>.

ASCO, the U.S. Preventive Services Task Force, the National Comprehensive Cancer Network, the Society of Gynecologic Oncology, and the American College of Obstetricians and Gynecologists all recommend universal genetic counseling and testing for women diagnosed with epithelial ovarian cancer<sup>11</sup>. Available literature shows that genetic testing offers clinical benefits to the patients in terms of the use of targeted therapies, also family members can benefit by risk-reducing surgery if found to be carriers and if tested negative can be counseled that their lifetime risk of ovarian cancer is similar to general population<sup>12</sup>.

Recurrence is seen in more than 80% of cases with advanced disease whereas almost 25% of cases with early disease in ovarian cancer after complete clinical response following primary treatment. Secondary cytoreductive surgery can be considered if platinum-sensitive recurrence and complete cytoreduction can be achieved<sup>13</sup>.

HIPEC (Hyperthermic intraperitoneal chemotherapy) after complete or optimal cytoreductive surgery allows optimal exposure of the drug to the entire seroperitoneal surface and early treatment of (microscopic) residual disease before re-growth can occur. Heating the drug in solution form itself may have a direct cytotoxic effect. Various randomized trials have

shown the benefit of HIPEC in ovarian cancer<sup>14</sup>.

Borderline ovarian tumors (BOTs) have low malignant potential and account for 15% of epithelial ovarian tumors. Among borderline ovarian tumors, serous borderline tumors have a higher prevalence than mucinous borderline tumors<sup>15</sup>. In the present study, there were only 5.26% cases of borderline ovarian tumors and the majority were mucinous borderline tumors. The primary method of treatment of BOTs is surgery. More than a third of BOTs affect women of reproductive age who wish to preserve their fertility potential so fertility-sparing surgery with unilateral or bilateral salpingo-oophorectomy can be done. Cystectomy can be done after proper counseling as the risk of recurrence is higher after cystectomy than oophorectomy. For patients without fertility requirements, total hysterectomy and bilateral salpingo-oophorectomy are recommended. Patients with metastases should be treated with maximal resection of the tumor. Because of the poor response of BOTs to chemotherapy, adjuvant chemotherapy is generally not recommended<sup>16</sup>.

Malignant ovarian germ cell tumors account for about 5% of all malignant ovarian neoplasms and are extremely chemo sensitive. They are commonly seen in teenage girls and at the time of presentation, disease is usually confined to one ovary. Careful surgical staging with unilateral salpingo-oophorectomy is the treatment of choice. Even in the presence of metastatic disease - the contralateral ovary, fallopian tube, and uterus should be left in situ if there is a desire to preserve fertility. Bleomycin, etoposide and cisplatin combination chemotherapy is regarded as the gold standard for adjuvant therapy<sup>17</sup>. Squamous cell carcinoma arising in mature cystic teratoma is a rare malignancy mainly occurring in older age. Hysterectomy and platinum-based chemotherapy improves survival<sup>18</sup>.

## Conclusion

Epithelial ovarian cancer is a lethal gynecological malignancy. Primary debulking surgery followed by platinum-based chemotherapy is the standard treatment. Available literature suggests the role



of HIPEC, targeted therapies, and genetic testing in ovarian cancer. Borderline ovarian tumors are common in women of reproductive age 30-40s whereas germ cell malignancies are common in younger girls below 20 years.

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