Oncol Ther (2022) 10:55–73
https://doi.org/10.1007/s40487-021-00179-9

REVIEW

# Efficacy and Safety of Platinum-Based Chemotherapy for Ovarian Cancer During Pregnancy: A Systematic Review and Meta-Analysis

Yaping Pei · Yuanfeng Gou · Na Li · Xiaojuan Yang · Xue Han · Liu Huiling

Received: August 23, 2021 / Accepted: November 17, 2021 / Published online: December 4, 2021


## ABSTRACT

***Introduction***: Based on the available data on ovarian cancer during pregnancy, we performed a review and meta-analysis to evaluate the efficacy and safety of platinum-based chemotherapy against ovarian cancer during pregnancy.
***Methods***: We systematically searched three databases including the PubMed, Embase, and Cochrane Library databases for articles published from January 1986 to December 2020 using the following terms: "ovarian tumors OR ovarian carcinoma OR adnexal masses OR ovarian cancer" AND "pregnancy" AND "chemotherapy." Two authors (Yaping Pei and Yuanfeng Gou) independently searched the literature and extracted data from each eligible study. The outcome measures were overall survival (OS) and progression-free survival (PFS). The OS and PFS of all patients were estimated by Kaplan–Meier survival curves and log-rank tests.
***Results***: A total of 43 studies including 55 cases of ovarian cancer during pregnancy were selected. Forty-eight patients were comprehensively staged using the International Federation of Gynecology and Obstetrics (FIGO) staging system. Twenty-six of the 48 patients (54.17%) were diagnosed with early-stage disease, while the remaining had advanced stages (II, III, and IV). The mean age at diagnosis was 29.31 years. The majority of patients in this meta-analysis were diagnosed at a mean gestational age of 16.05 weeks. The mean GA at chemotherapy administration was 17.42 weeks. Overall, 55 women gave birth to 56 newborns, including a pair of twins. At the end of follow-up (median 10 months, range 0–73 months), all the children were healthy, except for one child who died 5 days after delivery due to a congenital abnormality. During 2–204 months of follow-up, there were five cases of recurrence, with no evidence of recurrence in the remaining cases. Unfortunately, one patient died 29 months after diagnosis. Neither median overall survival nor median progression-free survival was obtained.
***Conclusion***: Platinum-based chemotherapy may be a good choice for pregnant women with ovarian cancer who want to continue their pregnancy.

**Supplementary Information** The online version contains supplementary material available at https://doi.org/10.1007/s40487-021-00179-9.

Y. Pei · Y. Gou · N. Li · X. Yang
Department of Clinical Medicine, Gansu University of Traditional Chinese Medicine, Lanzhou 730000, China

X. Han · L. Huiling (✉)
Department of Gynecology and Obstetrics, Gansu Provincial Hospital, Donggang West Road, Lanzhou 730000, China
e-mail: Liuhuiling75@163.com

**Keywords:** Chemotherapy; Meta-analysis; Ovarian cancer; Pregnancy

**Key Summary Points**

The incidence of cancer during pregnancy is likely to increase due to the delay in childbearing and application of reproductive technology. Ovarian cancer ranks fifth among the most common malignant tumors diagnosed during pregnancy, with an incidence of 0.2–2% globally.

Based on the available data on ovarian cancer during pregnancy, we performed a review and meta-analysis to evaluate the efficacy and safety of platinum-based chemotherapy against ovarian cancer during pregnancy.

Platinum-based chemotherapy may be a potential approach for patients with early-International Federation of Gynecology and Obstetrics (FIGO)-stage ovarian cancer during pregnancy.

## INTRODUCTION

The incidence of cancer during pregnancy is likely to increase due to the delay in childbearing and the application of reproductive technology [1]. The incidence of ovarian cancer has been reported at rates varying from 0.15 to 5.7%. Most ovarian tumors are benign and a few are borderline, while malignant tumors are rare [2]. Ovarian cancer ranks fifth among the most common malignant tumors diagnosed during pregnancy, with an incidence of 0.2–2% globally [3]. Owing to its low incidence and particularity, the diagnosis and treatment process usually needs to comprehensively consider many factors, such as pathological type, stage, gestational age, maternal and fetal prognosis, and the wishes of patients and family members, which increases the difficulty in diagnosis and treatment. Although guidelines based on the Third International Consensus definitions were developed by the European Society for Medical Oncology in 2019, there are no relevant data from large randomized trials that provide standard treatment for ovarian cancer during pregnancy. The goal for pregnant patients with ovarian cancer is the same as for non-pregnant individuals: to improve progression-free survival and preserve fertility. In addition, maintaining the optimal balance between management of the mother's cancer and preserving fetal health is critical. Therefore, multidisciplinary teams including gynecologists, obstetricians, pathologists, chemotherapists, and pediatricians are needed to provide a comprehensive therapeutic strategy and individualized treatment for patients with ovarian cancer. Standard chemotherapy for ovarian cancer in cases without pregnancy include platinum-based chemotherapy followed by surgery; in particular the combination of carboplatin and paclitaxel is suggested. Systemic chemotherapy and surgery are not administered in the first trimester to avoid affecting fetal outcomes due to the higher risk of spontaneous abortion and congenital malformations. Fetal deformity rates of 14–19% have been reported with exposure to chemotherapy drugs in the early stage of pregnancy, whereas the rate with exposure in the second and third trimesters is similar to that in healthy pregnant women (1–6%) [4]. However, studies have shown that while chemotherapy in the second and third trimesters during pregnancy will not increase fetal mortality and deformity, it may increase the incidence of non-malformation disorders, such as fetal growth restriction, low birth weight, and preterm delivery. In addition, while the maternal disease is under control, the safety of the fetus exposed to chemotherapeutic drugs is unknown. Previous studies have found that although exposure in the second and third trimesters of pregnancy has little effect on teratogenicity, it increases the risk of intrauterine growth retardation, preterm delivery, low birth weight, and bone marrow toxicity [5]. The combination of carboplatin and paclitaxel is suggested for epithelial ovarian cancer (EOC) and malignant sex cord-stromal tumors during pregnancy. Bleomycin-etoposide-cisplatin chemotherapy is

considered a preferred choice for ovarian malignant germ cell tumors. A cisplatin-vinblastine-bleomycin chemotherapy regimen may be used instead of etoposide, which increases the incidence of fetal intrauterine growth restriction and neonatal complications [6].

Although there is growing evidence in the literature for the use of chemotherapy during pregnancy, its safety remains uncertain. Therefore, the aim of this study was to conduct an up-to-date systematic review and meta-analysis to assess the efficacy and safety of chemotherapy and to describe pregnancy and maternal outcomes.

# METHODS

## Search Strategy

The PubMed, Embase, and Cochrane Library databases were searched for relevant articles published in English from January 1986 to December 2020. The search strategy including the following terms: ovarian tumors OR ovarian carcinoma OR adnexal masses OR ovarian cancer AND pregnancy AND chemotherapy. The references of all relevant reviews retrieved were also examined to prevent the omission of qualified studies. References to related articles were also searched to determine studies that might meet the criteria. The selection of all relevant studies was conducted independently by two authors (Yaping Pei and Yuanfeng Gou), and differences were resolved together.

## Inclusion Criteria

The inclusion criteria were as follows: women diagnosed with primary ovarian cancer during pregnancy; all published prospective and retrospective studies and case reports providing patient-relevant information; use of chemotherapy drugs during pregnancy. In the case of duplicates in the literature, the most recent and comprehensive articles were selected.

## Exclusion Criteria

Studies were excluded for any of the following reasons: pregnant women without ovarian cancer or metastatic ovarian cancer; studies that were books or reviews; no chemotherapy drugs were given during pregnancy; incomplete data.

## Data Extraction

Study information was gathered as follows: first author, publication year, patient age at diagnosis, gestational age (GA) at diagnosis, pathological type, International Federation of Gynecology and Obstetrics (FIGO) stage, grade, GA at chemotherapy administration, chemotherapy regimens during pregnancy and cycles, treatment during pregnancy, adverse events during pregnancy assessed using the National Cancer Institute Common Terminology Criteria for Adverse Events version 5 (CTCAE v5.0) [7], tumor size, GA at delivery, method of delivery, treatment after pregnancy, lymph node status, recurrence, fetal outcome, weight at delivery, follow-up period, overall survival (OS) in months, progression-free survival(PFS) in months, and outcomes for women.

## Statistical Analysis

Missing data were not included in the statistical analysis, and the number of missing data were indicated for each evaluation result. The quantitative synthesis of the published articles was divided into two parts. First, for data that were normally distributed, the classification data were described by frequency and percentage and count data (mean and standard deviation), respectively, while non-normally distributed data were described by median and range. Second, the OS and PFS of all cases were estimated by Kaplan–Meier survival curves. The log-rank test was used for the comparison between different subgroups, including chemotherapeutic drugs, FIGO stages, and pathological types. All statistical analyses were performed with GraphPad Prism 5.0 (GraphPad Software, Inc., La Jolla, CA, USA), and a value of $P < 0.05$ was considered indicative of statistical significance.

This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors. Therefore the study complies with ethics guidelines.

## RESULTS

A flow chart showing the stages of the search strategy is presented in Fig. 1. Following this strategy, a total of 3022 potential studies were searched and 2744 were excluded because of duplicates or irrelevance (based on titles and abstracts), using EndNote X9 software. Finally, 278 articles met the inclusion criteria. After full-text assessment, 228 articles were excluded because they were reviews, and five articles were excluded because no platinum-based treatment was used. Ultimately, 45 papers remained. However, the full text for two articles could not be found after much effort. As a result, 43 articles including 55 cases were eligible for the present study [8–50].

### Characteristics of Patients at Diagnosis

The detailed characteristics of all patients are shown in Table 1. Three patients were of unknown age at diagnosis of ovarian cancer, with a mean age of 29.31 years (SD 9.87, range 18–43). The mean GA at the time of ovarian cancer diagnosis was 16.05 (SD 7.72, range 7–29) weeks. Of the 55 cases, most were diagnosed in the second trimester of pregnancy (77.55%); eight were diagnosed during the first trimester (16.33%) and three during the third trimester (6.12%), while data were missing in six. The FIGO stage at diagnosis during pregnancy was early (stage I) in 54.17% (26 of 48) of women, and the remaining were advanced (stages II, III, IV). Among 52 patients with ovarian cancer during pregnancy, 53.85% were diagnosed with EOC (28 of 52) versus 46.15% (24 of 52) with non-EOC (NEOC), and data in three cases were lost.

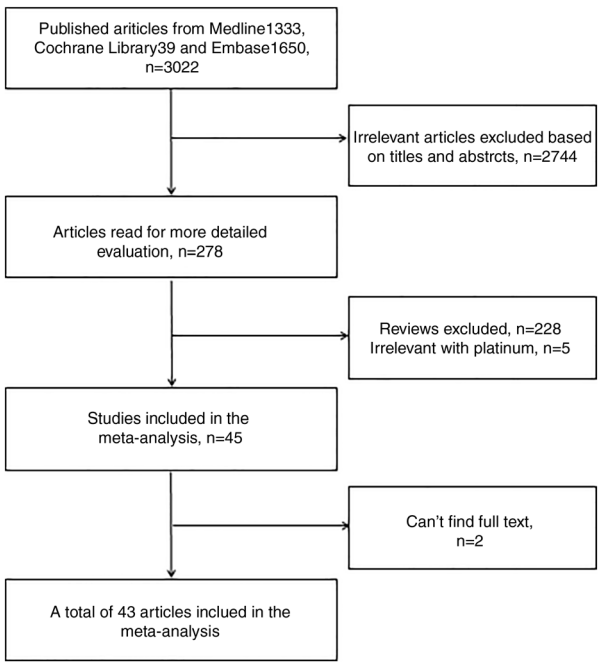


**Fig. 1** Flow chart of study selection in this meta-analysis

**Table 1** Summary studies describing of adjuvant platinum-based chemotherapy for ovarian cancer during pregnancy

| Author | Age at diagnosis (years) | GA at diagnosis (weeks) | Pathological type | FIGO Stage | GA at chemotherapy (weeks) | Agent | Treatment during pregnancy | Adverse effects | Response | Way of delivery |
|---|---|---|---|---|---|---|---|---|---|---|
| Malone [8] | 25 | 25 | York sac tumor | IC | 27 | Cisplatin + vinblastine + bleomycin,2cycles | USO | Nausea,vomiting,alopecia | NA | CD |
| Christman [9] | 29 | 15 | Immature teratoma | IC | 19 | Cisplatin + vinblastine + bleomycin,1cycles | USO | None | Serum AFP levels decreased significantly | VD |
| Malfetano [10] | 28 | 16 | Serous adenocarcinoma | IIIC | NA | Cyclophosphamide + cisplatin,q21d,7cycles | USO,OME | Nausea,vomiting | NA | VD |
| King [11] | 24 | 15.5 | Serous adenocarcinoma | IIIC | 16 | Cyclophosphamide + cisplatin,5cycles | USO,OME | Nausea,vomiting, neutrophil count decreased | NA | VD |
| Buller [12] | 21 | 26 | Dysgerminoma | IVB | 27 | Etoposide + cisplatin,4cycles | USO,OME | NA | Serum CA125,LDHlevels decreased significantly | VD |
| Henderson [13] | 40 | 17 | Serous adenocarcinoma | NA | 20 | Cyclophosphamide + cisplatin,2 ycles, Carboplatin + Cyclophosphamide | USO | Hearing impaired | NA | CD |
| Horbelt [14] | 18 | 20 | Immature teratoma and York sac tumor | IA | 21 | Bleomycin + etoposide + cisplatin,q28d,3cycles | USO | None | Serum AFP levels decreased significantly | VD |
| Koc [15] | 41 | 18 | Endometrioid adenocarcinoma | NA | 22 | Carboplatin,q28d,3cycles | USO,OME | None | NA | CD |
| Elit [16] | 26 | 23 | York sac tumor | IIC | 25 | Bleomycin + etoposide + cisplatin,q21d,1cycles | USO | None | NA | CD |
| Malhotra [17] | 19 | 15 | York sac tumor | IIIC | 18 | Bleomycin + etoposide + cisplatin,2cycles | None | NA | NA | CD |
| Ohara [18] | 22 | 16 | Serous adenocarcinoma | III | 18 | Cyclophosphamide + adriamycin + cisplatin,4cycles | USO | None | NA | CD |
| Otton [19] | 31 | 16 | Serous adenocarcinoma | NA | 18 | Cisplatin,q21d,4cycles | OCE | Anemia | Serum CA125 levels decreased significantly | CD |
| Sood [20] | 33 | 27 | Serous adenocarcinoma | IIIC | 28 | Paclitaxel + cisplatin,q21d,3cycles | USO,OME | Neutrophil count decreased,alopecia, nausea,vomiting | Serum CA125 levels decreased significantly | CD |
| Mendez [21] | 30 | 7.5 | Serous adenocarcinoma | IIIC | 16 | Paclitaxel + carboplatin.q21d,6cycles | USO,OME | None | Serum CA125 levels decreased significantly | CD |

**Table 1** continued

| Author | Age at diagnosis (years) | GA at diagnosis (weeks) | Pathological type | FIGO Stage | GA at chemotherapy (weeks) | Agent | Treatment during pregnancy | Adverse effects | Response | Way of delivery |
|---|---|---|---|---|---|---|---|---|---|---|
| Picone [22] | 43 | 22 | Endometrioid adenocarcinoma | IIIB | 27 | Carboplatin,q21d,2cycles | USO | None | Serum CA125 levels decreased significantly | CD |
| Ferrandina [23] | 40 | 15 | Serous adenocarcinoma | IIIC | 17 | Cisplatin,q21d,6cycles | BSO,OME,AE | Neutrophil count decreased,nausea,vomiting | Serum CA125 levels decreased significantly | CD |
| Han [24] | 25 | 20 | York sac tumor | IC | 22 | Bleomycin + etoposide + cisplatin,5cycles | USO,OME | None | NA | VD |
| Han [24] | 27 | 26 | Immature teratoma | IA | 30 | Bleomycin + etoposide + cisplatin,2cycles | USO | None | NA | VD |
| Schmeler [25] | 39 | 7 | Mucinous adenocarcinoma | IC | NA | Na | USO | NA | NA | NA |
| Schmeler [25] | 31 | 7 | Endometrioid adenocarcinoma | IC | NA | Na | USO | NA | NA | NA |
| Schmeler [25] | 22 | 9 | Dysgerminoma and endodermal sinus | IA | NA | Na | USO | NA | NA | NA |
| Hubalek [26] | 33 | 25 | Dysgerminoma | IC | 25 | Paclitaxel + carboplatin,q21d,3cycles | None | Nausea,alopecia | Serum CA125 levels decreased significantly | CD |
| Machado [27] | 22 | 13 | Dysgerminoma | IC | NA | Cisplatin + etoposide,5cycles | USO | NA | NA | NA |
| Machado [27] | 35 | 18 | York sac tumor | IC | NA | Cisplatin + etoposide,5cycles | BSO | NA | NA | NA |
| Modares [28] | 42 | 20 | Serous adenocarcinoma | IIIC | 22 | Paclitaxel + carboplatin.q21d,4cycles | USO,OME | None | Serum CA125 levels decreased significantly | CD |
| Motegi [29] | 33 | 18 | York sac tumor | IC | 19 | Cisplatin + vinblastine + bleomycin,3cycles | USO,OME | Platelet count decreased | NA | CD |
| Robova [30] | 34 | 21 | York sac tumor | IC | 22 | Cisplatin,q21d,4cycles | USO,OME | None | Serum AFP levels decreased significantly | CD |
| Karimi [31] | 26 | 28 | Immature teratoma | IIIC | 29 | Bleomycin + etoposide + cisplatin,q21d,2cycles | USO,OME | None | NA | CD |
| Poujade [32] | 36 | 22 | Immature teratoma | NA | 23 | Etoposide + cisplatin,q21d,3cycles | USO | None | NA | CD |

**Table 1** continued

| Author | Age at diagnosis (years) | GA at diagnosis (weeks) | Pathological type | FIGO Stage | GA at chemotherapy (weeks) | Agent | Treatment during pregnancy | Adverse effects | Response | Way of delivery |
|---|---|---|---|---|---|---|---|---|---|---|
| Tabata [33] | 34 | 18 | Undifferentiated carcinoma | IC | 21 | Carboplatin,q21d,4cycles | BSO | None | Serum CA125 levels decreased significantly | CD |
| Abellar [34] | 40 | NA | Mucinous adenocarcinoma | NA | 24 | Cisplatin | NA | Fetal growth retardation | NA | NA |
| Abellar [34] | 37 | NA | Clear cell carcinoma | NA | 24 | Cisplatin | NA | None | NA | NA |
| Doi [35] | 36 | 15 | Mucinous adenocarcinoma | IC | 24 | Carboplatin + paclitaxel,q14d,5cycles | USO | Fatigue | Serum CA125 levels decreased significantly | CD |
| Ghaemmaghami [36] | 25 | 21 | Immature teratoma | NA | 21 | Bleomycin + etoposide + cisplatin,3cycles | USO | None | NA | CD |
| Rouzi [37] | 32 | 20 | Serous adenocarcinoma | IIIC | 21 | Cisplatinum + docetaxel,q21d,4cycles | USO,OME | None | Serum CA125 levels decreased significantly | CD |
| Benjapibal [38] | 23 | 13 | York sac tumor | IC | 15 | Bleomycin + etoposide + cisplatin,q21d,4cycles | USO,OME | None | Serum AFP levels decreased significantly | CD |
| Barut [39] | 21 | 22 | Mucinous adenocarcinoma | IA | 25 | Carboplatin,q21d,3cycles | USO | NA | NA | VD |
| Serkies [40] | 24 | 28 | Mucinous adenocarcinoma | IV | 30 | Paclitaxel + cisplatin,q21d,2cycles | BSO,OME,AE | None | NA | CD |
| Viana [41] | 20 | 14 | York sac tumor | IIIC | 15 | Etoposide + cisplatin,6cycles | USO | None | Serum AFP,LDH levels decreased significantly | CD |
| Cardonick [42] | NA | 7 | NA | I | 8 | Carboplatin + paclitaxel | NA | Fetal growth retardation | NA | NA |
| Cardonick [42] | NA | 16 | NA | I | 22 | Cisplatin + paclitaxel | NA | None | NA | NA |
| Cardonick [42] | NA | 18 | NA | I | 24 | Carboplatin + paclitaxel | NA | None | NA | NA |
| Dobashi [43] | 33 | 17 | York sac tumor | IC | NA | Cisplatin + vincristin + bleomycin,4cycles | USO,OME | NA | NA | CD |
| Ruiz [44] | 42 | 15 | Clear cell carcinoma | III | 16 | Paclitaxel + carboplatin,q21d,6cycles | USO,AE | NA | Serum CA125, CA199 levels decreased significantly | CD |

**Table 1** continued

| Author | Age at diagnosis (years) | GA at diagnosis (weeks) | Pathological type | FIGO Stage | GA at chemotherapy (weeks) | Agent | Treatment during pregnancy | Adverse effects | Response | Way of delivery |
|---|---|---|---|---|---|---|---|---|---|---|
| Smith [45] | 36 | 12 | Serous adenocarcinoma | IIB | 14 | Carboplatin + paclitaxel,q28d,6cycles | USO,OME,PALNE,AE | Vomiting,anemia,platelet count decreased,nausea | NA | CD |
| Chen [46] | 36 | 14 | Endometrioid adenocarcinoma | IC | 18 | Paclitaxel + carboplatin,q21d,5cycles | USO | Nausea,alopecia,vomiting | Serum CA125 levels decreased significantly | CD |
| Hummeida [47] | 37 | 18 | Small cells ovarian cancer | IIIC | 19 | Cyclophosamide + carboplatin,q28d,6cycles | BSO,OME,AE | NA | Serum CA125 levels decreased significantly | CD |
| Luh [48] | 31 | 19 | Immature teratoma | IC | 28 | Cisplatin + etoposide + bleomyci,4cycles | USO,OME | NA | NA | VD |
| Luh [48] | 24 | 29 | Dysgerminoma | IC | 34 | Cisplatin + etoposide + bleomyci,4cycles | USO,OME | NA | NA | VD |
| Luh [48] | 27 | 19 | York sac tumor | IC | 22 | Carboplatin + docetaxe,6cycles | USO,OME,AE | NA | NA | CD |
| Moro [49] | 29 | NA | Serous adenocarcinoma | IC | NA | Na | BSO | NA | NA | CD |
| Moro [49] | 40 | NA | Serous adenocarcinoma | IIIC | NA | Na | BSO | NA | NA | VD |
| Moro [49] | 42 | NA | Endometrioid adenocarcinoma | IIB | NA | Na | USO | NA | NA | CD |
| Moro [49] | 34 | NA | Serous adenocarcinoma | IIIA | NA | Na | USO | NA | NA | VD |
| Xu [50] | 34 | 20 | Serous adenocarcinoma | IIIC | 22 | Docetaxel + carboplatin,4cycles | BSO,OME | Dyspnea,ventricular tachycardia | Serum CA125, CA199 and HE4 levels decreased significantly | CD |

| Author | GA at delivery (weeks) | Treatment after pregnancy | Lymph nodes status | Recurrence | Maternal outcomes | OS(months) | PFS (months) | Weight at delivery(g) | Fetal outcome |
|---|---|---|---|---|---|---|---|---|---|
| Malone [8] | 32 | Chemo | Negative | No | NED | > 12 | > 12 | 1900 | Healthy at 18 months |
| Christman [9] | 40 | HYE,OME,PALNE,chemo | Negative | No | NED | > 59 | > 59 | 3232 | Healthy at 60 months |
| Malfetano [10] | 37 | HYE,BSO | Negative | No | NED | > 19 | > 19 | 3275 | Healthy at 19 months |
| King [11] | 36.5 | HYE,USO,OME,chemo | Negative | No | NED | > 28 | > 28 | 3060 | Healthy at 28 months |
| Buller [12] | 38 | None | Positive | No | NED | > 12 | > 12 | 2320 | Healthy at 9 months |

**Table 1** continued

| Author | GA at delivery (weeks) | Treatment after pregnancy | Lymph nodes status | Recurrence | Maternal outcomes | OS(months) | PFS (months) | Weight at delivery(g) | Fetal outcome |
|---|---|---|---|---|---|---|---|---|---|
| Henderson [13] | 36 | HYE,USO,OME,AE,PALNE,chemo | Positive | No | NED | > 20 | > 20 | 3600 | Healthy at 12 months |
| Horbelt [14] | 39 | None | Negative | No | NED | NA | NA | 2769 | Healthy at birth |
| Koc [15] | 37 | HYE,USO | Negative | NA | NED | NA | NA | 3245 | Healthy at birth |
| Elit [16] | 28 | Chemo | Negative | No | NED | > 17.25 | > 17.25 | 1085 | Ventriculomegaly,cerebral atrophy,healthy at1.7 months |
| Malhotra [17] | 31 | NA | NA | NA | DOD | NA | NA | NA | Healthy at birth |
| Ohara [18] | 33 | HYE,USO,AE,OME.chemo | Negative | No | NED | > 10 | > 10 | 1896 | Healthy at 10 months |
| Otton [19] | 31 | HYE,BSO,OME,PALNE,chemo | Negative | No | NED | > 15.75 | > 15.75 | 1740 | Healthy at 12 months |
| Sood [20] | 37 | HYE,USO,AE,PALNE,chemo | Negative | YES | DOD | 29 | 6.25 | 2800 | Healthy at 30 months |
| Mendez [21] | 35.5 | HYE,USO,AE,PALNE,chemo | Positive | No | NED | > 15 | > 15 | 2500 | Healthy at 15 months |
| Picone [22] | 34 | HYE,USO,OME,PALNE,AE,chemo | Negative | No | NED | > 18.25 | > 18.25 | 1900 | Healthy at 18 months |
| Ferrandina [23] | 36 | HYE,chemo | NA | YES | NED | > 50 | > 29.25 | 3000 | Healthy at 42 months |
| Han [24] | 40 | Chemo | Negative | No | NED | > 72 | > 72 | 2610 | Healthy at 72 months |
| Han [24] | 38 | PALNE,OME,chemo | Negative | No | NED | > 26 | > 26 | 2970 | Intussusception at7.5 months,healthy at26months |
| Schmeler [25] | NA | NA | NA | NA | NED | > 4 | > 4 | NA | Healthy at birth |
| Schmeler [25] | NA | NA | NA | NA | NED | > 132 | > 132 | NA | Healthy at birth |
| Schmeler [25] | NA | NA | NA | NA | NED | > 156 | > 156 | NA | Healthy at birth |
| Hubalek [26] | 35 | HYE,USO,OME,PALNE,chemo | Negative | No | NED | > 22 | > 22 | 2450 | Healthy at 20 months |
| Machado [27] | NA | USO | NA | No | NED | > 3 | > 3 | 3190 | Healthy at 60 months |
| Machado [27] | NA | NA | NA | No | NED | > 72 | > 72 | 2200 | Healthy at 24 months |
| Modares [28] | 35 | HYE,USO,OME,chemo | Negative | No | NED | > 12 | > 12 | 2600 | Healthy at 6 months |
| Motegi [29] | 31 | Chemo | Negative | No | NED | > 65.25 | > 65.25 | 1070 | Healthy at birth |
| Robova [30] | 35 | PALNE,HYE,USO,chemo | Negative | No | NED | > 28 | > 28 | 1980 | Healthy at 24 months |
| Karimi [31] | 39 | OME,chemo | Negative | No | NED | > 22.25 | > 22.25 | 3100 | Healthy at 18 months |
| Poujade [32] | 39 | USO,chemo | Negative | No | NED | > 11.75 | > 11.75 | 3130 | Healthy at birth |
| Tabata [33] | 33 | HYE,OME,PALNE,chemo | Negative | No | NED | > 19.5 | > 19.5 | 2222 | Healthy at 12 months |
| Abellar [34] | 39 | NA | NA | NA | NED | NA | NA | SGA | Healthy at birth |

**Table 1** continued

| Author | GA at delivery (weeks) | Treatment after pregnancy | Lymph nodes status | Recurrence | Maternal outcomes | OS(months) | PFS (months) | Weight at delivery(g) | Fetal outcome |
|---|---|---|---|---|---|---|---|---|---|
| Abellar [34] | 39 | NA | NA | NA | NED | NA | NA | AGA | Healthy at birth |
| Doi [35] | 36 | OME,PLNE | Negative | No | NED | > 40 | > 40 | 2062 | Healthy at 40 months |
| Ghaemmaghami [36] | 36 | OME,USO | Negative | No | NED | > 15.75 | > 15.75 | 2000 | mild glandular hypospadia, healthy at 8 months |
| Rouzi [37] | 34 | USO,HYE,OME,chemo | Negative | No | NED | > 11 | > 11 | 2245 | Death 5 days after the delivery(congenital anomalies diagnosed before starting chemotherapy) |
| Benjapibal [38] | 36 | None | Negative | No | NED | > 28.75 | > 28.75 | 1560 | Healthy at 21 months |
| Barut [39] | 33 | HYE,USO,AE,PALNE,chemo | Negative | No | NED | > 7.75 | > 7.75 | 2280 | Healthy at 7.75 months |
| Serkies [40] | 34 | Chemo | Positive | YES | DOD | 35 | 7 | 1900 | Healthy at 73 months |
| Viana [41] | 35 | USO | Negative | NO | NED | > 29.25 | > 29.25 | 2070 | Anemia,thrombocytopenia, relative lymphocytosis, healthy at 24 months |
| Cardonick [42] | 36 | NA | NA | NA | NED | NA | NA | 1886 | IUGR |
| Cardonick [42] | 38 | NA | NA | NA | NED | > 160 | NA | 2608;2623 | Twin A: normal; Twin B: jaundice; hyperbilirubinemia, Tourette's syndrome, dyslexia, Asperger's syndrome and speech delay |
| Cardonick [42] | 39 | NA | NA | NA | NED | > 38 | NA | 3629 | Healthy at 6 months |
| Dobashi [43] | 31 | NA | NA | NA | NED | > 36 | > 36 | NA | Healthy at birth |
| Ruiz [44] | 38 | Chemo | Positive | NA | NED | > 7.75 | > 7.75 | 2850 | Healthy at 2 months |
| Smith [45] | 37 | HYE,USO,chemo | Negative | NA | NED | > 9.5 | > 9.5 | 2126 | Birth with bilateralcongenital talipes equinovarus. healthy at7months |
| Chen [46] | 37 | NA | Negative | No | NED | > 18 | > 18 | 2888 | Healthy at 18 months |
| Hummeida [47] | 38 | HYE | Negative | No | NED | > 23 | > 23 | 2900 | Healthy at 18 months |
| Luh [48] | 41 | HYE,USO,OME,PALNE,AE,chemo | Negative | No | NED | > 10 | > 10 | 2700 | Healthy at 2 months |
| Luh [48] | 35 | HYE,USO,chemo | Negative | No | NED | > 24 | > 24 | 2105 | Healthy at 24 months |
| Luh [48] | 38 | HYE,USO,OME,chemo | Negative | No | NED | > 24 | > 24 | 3165 | Healthy at 24 months |

**Table 1** continued

| Author | GA at delivery (weeks) | Treatment after pregnancy | Lymph nodes status | Recurrence | Maternal outcomes | OS(months) | PFS (months) | Weight at delivery(g) | Fetal outcome |
|---|---|---|---|---|---|---|---|---|---|
| Moro [49] | 38 | None | NA | No | NED | > 14 | > 14 | 3650 | Healthy at birth |
| Moro [49] | 39 | Chemo,surgery(not detailed) | NA | YES | NED | > 204 | NA | 2980 | Healthy at birth |
| Moro [49] | 37 | HYE,USO,OME,PLNE | NA | No | NED | > 28 | > 28 | 2200 | Healthy at birth |
| Moro [49] | 36 | HYE,USO,AE | NA | No | NED | > 24 | > 24 | 2760 | Healthy at birth |
| Xu [50] | 35 | HYE,PALNE,AE,PSE,OME,chemo | Positive | YES | NED | > 30.25 | 25.75 | 2100 | Healthy at 33 months |

*AE* appendectomy; *BSO* bilateral salpingo-oophorectomy; *CD* cesarean delivery; Chemo chemotherapy; *DOD* death of disease; *GA* gestational age; *HYE* hysterectomy; *IUGR* intrauterine growth retardation; *NA* not available; *NED* no evidence of disease; *OCE* ovarian cystectomy; *OME* omentectomy; *OS* overall survival; *PALNE* pelvic-aortic lymphadenectomy; *PFS* profession-free survival; *PLNE* pelvic lymphadenectomy; *PSE* partial sigmoidectomy; *USO* unilateral salpingo-oophorectomy; *VD* vaginal delivery

## Patient Management During Pregnancy

Detailed data on GA at the start of chemotherapy were available for only 44 women. Except for one patient who received chemotherapy at 8 weeks, all patients began treatment in the second or third trimester of pregnancy. The mean GA at chemotherapy administration was 17.42 (SD 9.88, range 8–34) weeks. Nine patients (18.75%) received platinum alone; 39 patients received combination drugs, including paclitaxel (15 patients), etoposide (5), cyclophosphamide (4), bleomycin and etoposide (10), cyclophosphamide and doxorubicin (1), and vincristine with bleomycin (4). Of the 37 women for whom data were available, chemotherapy was well-tolerated by 22 patients during pregnancy. Unfortunately, the remaining 15 patients reported various types of adverse events including anemia, dyspnea, ventricular tachycardia, fatigue, fetal growth retardation, hearing impairment, nausea, alopecia, vomiting, decreased neutrophil count, and decreased platelet count. In addition, intrauterine fetal growth restriction occurred in two patients who started chemotherapy at 8 and 24 weeks of pregnancy [44, 53], respectively. One was diagnosed at 39 weeks of pregnancy, and no relevant information could be found for the other. Most patients underwent surgery during pregnancy, including bilateral salpingo-oophorectomy (BSO; 16.0%), unilateral salpingo-oophorectomy (USO; 78.0%) and ovarian cystectomy (OCE; 2.0%). Two patients did not undergo surgery, and such data were missing in five cases. It is not known whether there were alternative therapies after the operation. The response to chemotherapy is the change in tumor markers in serum, including cancer antigen 125 (CA-125), CA-199, alpha-fetoprotein (AFP), lactate dehydrogenase (LDH), and human epididymis protein 4 (HE4). In this study, these biomarkers decreased significantly in 20 cases.

## Patient Delivery

Data on mode of delivery and gestational age were available for 45 and 50 cases, respectively.

Thirty-three women (73.33%) underwent cesarean section, of which 28 were planned. Of the 12 women with vaginal delivery, six were spontaneous. The mean GA at delivery was 32.75 weeks (SD 10.78, range 28–41).

### Further Patient Treatment After Delivery and Maternal Outcomes

Information regarding further postpartum treatment was available in 43 cases. In 20 women, parturition and surgery were performed at the same time, and in nine cases surgery was performed following delivery. Hysterectomy was performed in 25 of 43 cases (58.14%), bilateral salpingo-oophorectomy was performed in two cases (4.65%), unilateral salpingo-oophorectomy was performed in 22 cases (51.16%), pelvic–aortic lymph node dissection was performed in 13 cases (30.23%), and pelvic lymph node dissection was performed in two cases. In addition, nine patients underwent appendectomy, and 69.77% underwent further chemotherapy. Four patients received neither surgery nor chemotherapy after delivery. Of the 38 patients for whom lymph node status was available, six showed evidence of positive lymph nodes. Among the available data, there were five cases of recurrence, and no evidence of recurrence was reported in the remaining patients. Unfortunately, one patient died 29 months after diagnosis. Twenty-eight cases reported no gross residual disease at the conclusion of surgery.

### Neonatal Outcomes

A total of 56 babies were born, including one set of twins. Forty-nine babies were born completely healthy; the other seven neonates showed the following conditions: ventriculomegaly cerebral atrophy (1); intussusception (1); mild glandular hypospadias (1); jaundice, hyperbilirubinemia, Tourette's syndrome, dyslexia, Asperger's syndrome, and speech delay (1); bilateral congenital talipes equinovarus (1); anemia, thrombocytopenia, and relative lymphocytosis (1); and intrauterine growth retardation (1). The mean weight of newborns at delivery was 2198.77 g (SD 1015.32, range 1070–3650 g), while no relevant data were available for seven newborns. At the end of follow-up (median 10 months, range 0–-73 months), all newborns with available data were healthy except one, who died due to congenital abnormalities 5 days after delivery. In the case of twins, one of the babies was born with jaundice and hyperbilirubinemia and was subsequently diagnosed with dyslexia, speech retardation, Asperger's syndrome, and Tourette's syndrome.

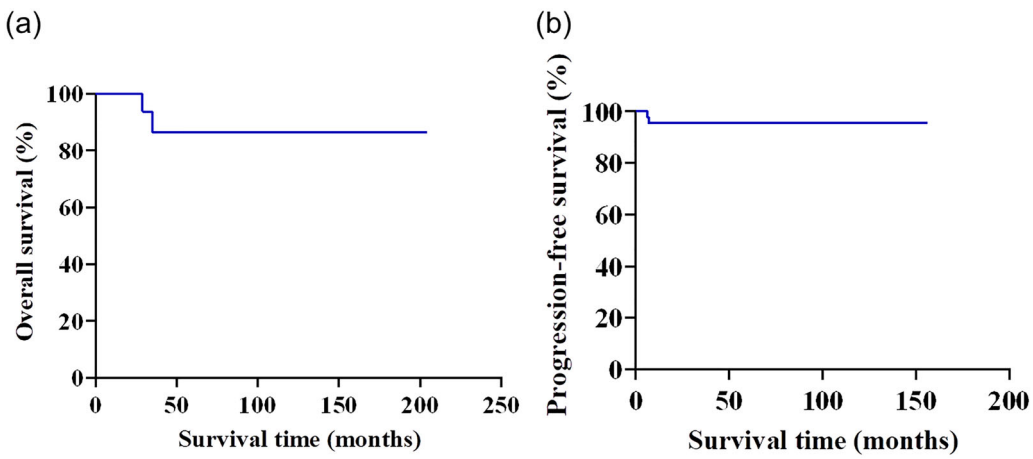


**Fig. 2** Kaplan–Meier survival curves. **a** Overall survival, $n = 49$. **b** Progression-free survival, $n = 46$

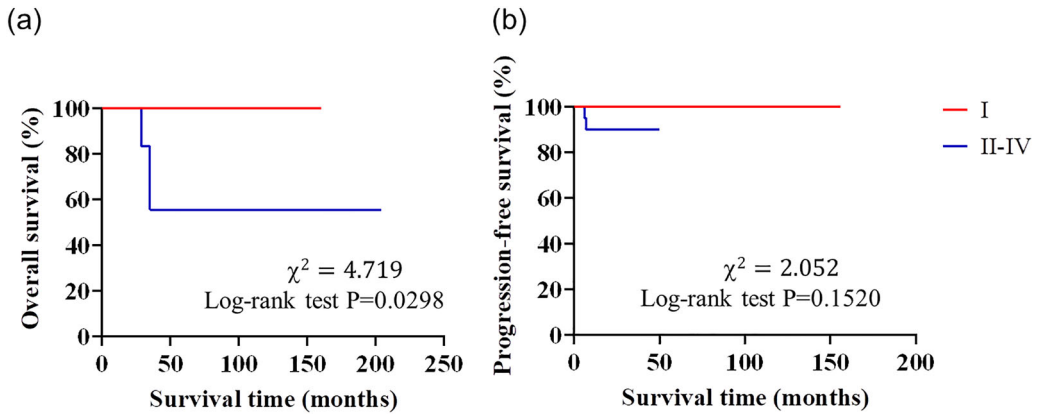


**Fig. 3** Kaplan–Meier survival curves by FIGO stage. **a** Overall survival, I, $n = 24$; II–IV, $n = 21$. **b** Progression-free survival, I, $n = 22$; II–IV, $n = 20$

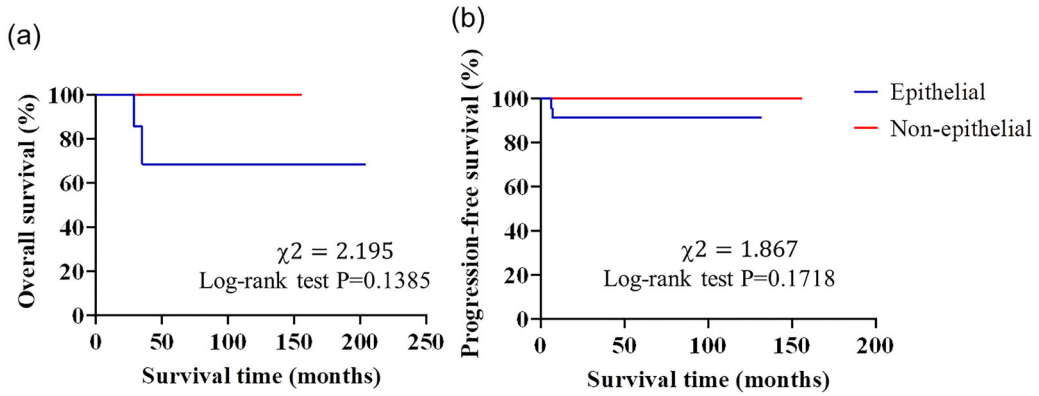


**Fig. 4** Kaplan–Meier survival curves by pathological type. **a** Overall survival: epithelial, $n = 25$; non-epithelial, $n = 22$. **b** Progression-free survival: epithelial, $n = 24$; non-epithelial, $n = 22$

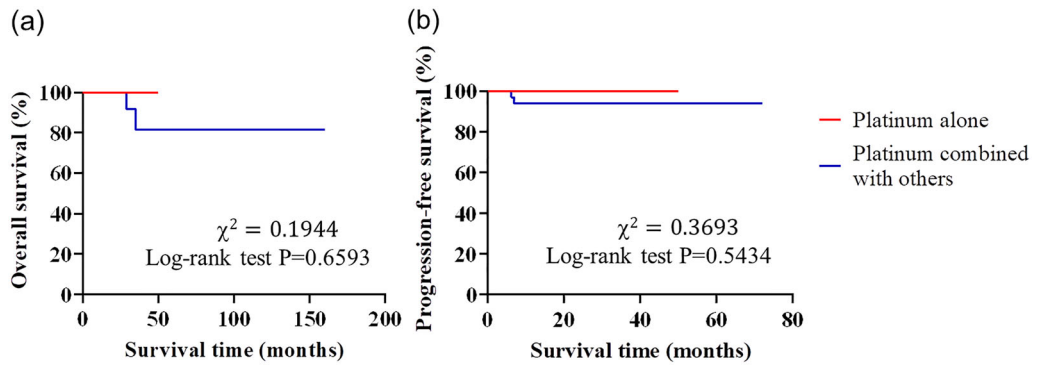


**Fig. 5** Kaplan–Meier survival curves by FIGO stage. **a** Overall survival: platinum alone, $n = 6$; platinum combination, $n = 36$. **b** Progression-free survival: platinum alone, $n = 6$; platinum combination, $n = 34$

### Survival Analysis

OS and PFS were assessed for all patients after receiving platinum-based chemotherapy during pregnancy. Kaplan–Meier curves for OS and PFS are shown in Fig. 2. Of the 49 women for whom relevant data were obtained, 47 were still alive at the end of follow-up (median 22 months, range 2–204 months). As a result, median OS was not calculated because the cumulative survival rate was greater than 50% (Fig. 2a), and the same was true for PFS (Fig. 2b). Because various chemotherapeutic drugs, different pathological types, and FIGO-stage diagnosis of ovarian cancer may have an impact on OS and PFS, subgroup analysis was further carried out with log-rank tests for FIGO stage, pathological type, and chemotherapy regimen. As shown in Fig. 3, compared with an advanced stage, better prognosis was associated with early-stage disease (OS: log-rank $\chi^2 = 4.719$, $P = 0.0298$; PFS: log-rank $\chi^2 = 2.052$, $P = 0.1520$). However, there was no significant difference between EOC and NEOC in OS and PFS (Fig. 4, OS: log-rank $\chi^2 = 2.195$, $P = 0.1385$; PFS: log-rank $\chi^2 = 1.867$, $P = 0.1718$). Similarly, the log-rank test failed to detect any significant difference in OS or PFS between platinum alone and combination therapy (Fig. 5, OS: log-rank $\chi^2 = 0.1944$, $P = 0.6593$; PFS: log-rank $\chi^2 = 0.3693$, $P = 0.5434$).

## DISCUSSION

Ovarian cancer ranks fifth among the most common malignant tumors diagnosed during pregnancy, with reported incidence varying from 0.2 to 2% [3]. According to reported evidence, ovarian cancer ranks sixth in the Asian population [51]. Like ovarian cancer in non-pregnant patients, gestational ovarian cancer is diagnosed by intraoperative or postoperative pathology [52]. Although the proper management of ovarian cancer in pregnant women has been established, its scientific proof is relatively weak. For pregnant women with ovarian cancer who choose to continue pregnancy, treatment includes surgical staging and tumor reduction surgery followed by chemotherapy, timely delivery, and chemotherapy after surgery. In order to reduce the risk of miscarriage, torsion, rupture, and delayed diagnosis of malignant tumors, surgery should be performed in the second trimester of pregnancy [6]. In the present study, fertility-sparing surgery was performed during pregnancy for six cases during the first trimester, 27 in the second trimester, and one in the third trimester, while eight women underwent BSO, and two underwent no surgery.

As a pregnancy category D drug listed by the Food and Drug Administration (FDA), chemotherapeutic drugs have obvious risks to the fetus. However, several studies have indicated that the use of anticancer agents during pregnancy is feasible, not only in ovarian cancer, but also in leukemia, lymphoma, colon cancer, breast cancer, gastric cancer, cervical cancer, sarcoma, and lung cancer [53–60]. In the present study, at the end of follow-up (median 10 months, range 0–73 months), all newborns with available data were healthy except one who died due to congenital abnormalities 5 days after delivery. Of the twins who were exposed to the same chemotherapy in utero, one developed normally and reportedly did well in school [42].

It is well known that the main factors affecting the prognosis of ovarian cancer are stage and pathological type [61]. In this study, 26 women received chemotherapy in the early stage. Compared with the advanced stage, early-stage treatment obviously had a more favorable prognosis. With regard to the type of ovarian cancer, EOC represents the vast majority of cases in comparison with NEOC [62]. In addition, NEOC, especially malignant germ cell tumors, is more sensitive to chemotherapy [63]. However, prognostic analysis based on pathological type in this study showed that there was no significant difference between EOC and NEOC, and no significant differences in OS and PFS were observed based on log-rank tests in these two stratified analyses. This result may be due to the small number of studies. Therefore, additional studies with larger samples is recommended in the future. In addition to focusing on the effects of drugs on developing fetuses and the long-term effects of intrauterine

exposure on offspring, we also need to pay more attention to the health of pregnant women, including OS and PFS.

Through a retrospective study over 35 years, we found that 55 cases of ovarian cancer diagnosed during pregnancy were treated with platinum-based chemotherapy, and five cases [64–68] were treated with another chemotherapy regimen. With the exception of one patient who received chemotherapy at 8 weeks, all patients began treatment in the second or third trimester of pregnancy. Like non-pregnant patients, various chemotherapy-induced adverse effects were observed in pregnant women, including nausea, vomiting, anemia, dyspnea, ventricular tachycardia, and fatigue. Pregnancy complications including fetal ventriculomegaly, intrauterine growth restriction, and fetal bilateral ventriculomegaly were noted. Analysis of prognosis on the basis of chemotherapy regimen revealed no significant difference between platinum alone and platinum combination. Because the cumulative survival rate was greater than 50%, the median OS and PFS were not reached. These results indicate that platinum-based chemotherapy may be a safe approach in most cases of ovarian cancer in the second and third trimesters of pregnancy.

Most individual studies did not provide detailed data relating to each woman's survival or other basic characteristics (such as the pathological type of cancer or GA at diagnosis and delivery). In addition, the long-term outcomes for these infants are unknown, and the median follow-up time was short. As a result, neither descriptive statistics nor survival analysis could be performed on the included cases, which reduces the reliability of this meta-analysis. Nevertheless, the strength of our study is that the analysis included the largest sample size ever used to assess pregnancy outcomes for ovarian cancer. Therefore, it is strongly recommended that larger population-based studies be conducted in the future. In short, platinum-based chemotherapy may be a good choice for pregnant women with ovarian cancer who want to continue their pregnancy.

## CONCLUSION

Taken together, our results suggest that platinum-based chemotherapy may be an appropriate therapy for pregnant women with ovarian cancer in the second and third trimesters. Tumor stage, lymph node metastasis, gestational age, general condition, fetal maturity, and other factors should be considered in the treatment. Currently, there is no standard treatment for gestational ovarian cancer. Most of the treatments are available for non-gestational ovarian cancer. However, the efficacy and effects of related treatment on the prognosis of pregnant women and fetuses are also controversial, and there is no unified conclusion at present. Therefore, there is an urgent need for reliable data from studies with large samples and long-term follow-up to guide clinical treatment to maximize maternal and fetal outcomes.

## ACKNOWLEDGEMENTS

***Funding.*** This research, including the journal's Rapid Service fees, was supported by the Natural Science Foundation of Gansu Province in China (No. 21JR1RA018).

***Authorship.*** All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published.

***Author Contributions.*** Yaping Pei and Yuanfeng Gou: project development, data collection, manuscript writing and editing. Huiling Liu and Na Li: project development, data analysis, manuscript editing. Xiaojuan Yang and Xue Han: project development. Huiling Liu manuscript revisions.

***Disclosures.*** Yaping Pei, Yuanfeng Gou, Na Li, Xiaojuan Yang, Xue Han, and Huiling Liu all confirm that they have no conflicts of interest to declare.

***Compliance with Ethics Guidelines.*** This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

***Data Availability.*** All data generated or analyzed during this study are included in this published article/as supplementary information files.



## REFERENCES

1. Pavlidis N. Cancer and pregnancy: what should we know about the management with systemic treatment of pregnant women with cancer? Eur J Cancer. 2011;47(Suppl 3):S348-352.
2. Mukhopadhyay A, Shinde A, Naik R. Ovarian cysts and cancer in pregnancy. Best Pract Res Clin Obstet Gynaecol. 2016;33:58–72.
3. Fruscio R, de Haan J, Van Calsteren K, et al. Ovarian cancer in pregnancy. Best Pract Res Clin Obstet Gynaecol. 2017;41:108–17.
4. Backes CH, Moorehead PA, Nelin LD. Cancer in pregnancy: fetal and neonatal outcomes. Clin Obstet Gynecol. 2011;54:574–90.
5. Zheng X, Zhu Y, Zhao Y, et al. Taxanes in combination with platinum derivatives for the treatment of ovarian cancer during pregnancy: a literature review. Int J Clin Pharmacol Ther. 2017;55:753–60.
6. The NCCN ovarian cancer chinicsl practice guidelines in ovarian cancer, Version 1. February 26, 2021.
7. Cancer Therapy Evaluation Program (CTEP) of the National Cancer Institute (NCI). Common Terminology Criteria for Adverse Events (CTCAE) v50 US Department of Health and Human Services. Bethesda: National Institutes of Health, National Cancer Institute; 2017.
8. Malone JM, Gershenson DM, Creasy RK, et al. Endodermal sinus tumor of the ovary associated with pregnancy. Obstet Gynecol. 1986;68:86s–9s.
9. Christman JE, Teng NN, Lebovic GS, et al. Delivery of a normal infant following cisplatin, vinblastine, and bleomycin (PVB) chemotherapy for malignant teratoma of the ovary during pregnancy. Gynecol Oncol. 1990;37:292–5.
10. Malfetano JH, Goldkrand JW. Cis-platinum combination chemotherapy during pregnancy for advanced epithelial ovarian carcinoma. Obstet Gynecol. 1990;75:545–7.
11. King LA, Nevin PC, Williams PP, et al. Treatment of advanced epithelial ovarian carcinoma in pregnancy with cisplatin-based chemotherapy. Gynecol Oncol. 1991;41:78–80.
12. Buller RE, Darrow V, Manetta A, et al. Conservative surgical management of dysgerminoma concomitant with pregnancy. Obstet Gynecol. 1992;79:887–90.
13. Henderson CE, Elia G, Garfinkel D, et al. Platinum chemotherapy during pregnancy for serous cystadenocarcinoma of the ovary. Gynecol Oncol. 1993;49:92–4.
14. Horbelt D, Delmore J, Meisel R, et al. Mixed germ cell malignancy of the ovary concurrent with pregnancy. Obstet Gynecol. 1994;84:662–4.
15. Koc ON, McFee M, Reed E, et al. Detection of platinum-DNA adducts in cord blood lymphocytes following in utero platinum exposure. Eur J Cancer. 1994;30a:716–7.
16. Elit L, Bocking A, Kenyon C, et al. An endodermal sinus tumor diagnosed in pregnancy: case report and review of the literature. Gynecol Oncol. 1999;72:123–7.
17. Malhotra N, Sood M. Endodermal sinus tumor in pregnancy. Gynecol Oncol. 2000;78:265–6.

18. Ohara N, Teramoto K. Successful treatment of an advanced ovarian serous cystadenocarcinoma in pregnancy with cisplatin, adriamycin and cyclophosphamide (CAP) regimen case report. Clin Exp Obstet Gynecol. 2000;27:123–4.

19. Otton G, Higgins S, Phillips KA, et al. A case of early-stage epithelial ovarian cancer in pregnancy. Int J Gynecol Cancer. 2001;11:413–7.

20. Sood AK, Shahin MS, Sorosky JI. Paclitaxel and platinum chemotherapy for ovarian carcinoma during pregnancy. Gynecol Oncol. 2001;83: 599–600.

21. Méndez LE, Mueller A, Salom E, et al. Paclitaxel and carboplatin chemotherapy administered during pregnancy for advanced epithelial ovarian cancer. Obstet Gynecol. 2003;102:1200–2.

22. Picone O, Lhommé C, Tournaire M, et al. Preservation of pregnancy in a patient with a stage IIIB ovarian epithelial carcinoma diagnosed at 22 weeks of gestation and treated with initial chemotherapy: case report and literature review. Gynecol Oncol. 2004;94:600–4.

23. Ferrandina G, Distefano M, Testa A, et al. Management of an advanced ovarian cancer at 15 weeks of gestation: case report and literature review. Gynecol Oncol. 2005;97:693–6.

24. Han JY, Nava-Ocampo AA, Kim TJ, et al. Pregnancy outcome after prenatal exposure to bleomycin, etoposide and cisplatin for malignant ovarian germ cell tumors: report of 2 cases. Reprod Toxicol. 2005;19:557–61.

25. Schmeler KM, Mayo-Smith WW, Peipert JF, et al. Adnexal masses in pregnancy: surgery compared with observation. Obstet Gynecol. 2005;105: 1098–103.

26. Hubalek M, Smekal-Schindelwig C, Zeimet AG, et al. Chemotherapeutic treatment of a pregnant patient with ovarian dysgerminoma. Arch Gynecol Obstet. 2007;276:179–83.

27. Machado F, Vegas C, Leon J, et al. Ovarian cancer during pregnancy: analysis of 15 cases. Gynecol Oncol. 2007;105:446–50.

28. Modares Gilani M, Karimi Zarchi M, Behtash N, et al. Preservation of pregnancy in a patient with advanced ovarian cancer at 20 weeks of gestation: case report and literature review. Int J Gynecol Cancer. 2007;17:1140–3.

29. Motegi M, Takakura S, Takano H, et al. Adjuvant chemotherapy in a pregnant woman with endodermal sinus tumor of the ovary. Obstet Gynecol. 2007;109:537–40.

30. Robova H, Rob L, Hrehorcak M, et al. Endodermal sinus tumor diagnosed in pregnancy: a case report. Int J Gynecol Cancer. 2007;17:914–6.

31. Karimi Zarchi M, Behtash N, Modares GM. Good pregnancy outcome after prenatal exposure to bleomycin, etoposide and cisplatin for ovarian immature teratoma: a case report and literature review. Arch Gynecol Obstet. 2008;277:75–8.

32. Poujade O, Pujade-Lauraine E, Levardon M, et al. Ovarian malignant immature teratoma associated with pregnancy–a case report. Eur J Gynaecol Oncol. 2008;29:649–50.

33. Tabata T, Nishiura K, Tanida K, et al. Carboplatin chemotherapy in a pregnant patient with undifferentiated ovarian carcinoma: case report and review of the literature. Int J Gynecol Cancer. 2008;18:181–4.

34. Abellar RG, Pepperell JR, Greco D, et al. Effects of chemotherapy during pregnancy on the placenta. Pediatr Dev Pathol. 2009;12:35–41.

35. Doi D, Boh Y, Konishi H, et al. Combined chemotherapy with paclitaxel and carboplatin for mucinous cystadenocarcinoma of the ovary during pregnancy. Arch Gynecol Obstet. 2009;280:633–6.

36. Ghaemmaghami F, Abbasi F, Abadi AG. A favorable maternal and neonatal outcome following chemotherapy with etoposide, bleomycin, and cisplatin for management of grade 3 immature teratoma of the ovary. J Gynecol Oncol. 2009;20: 257–9.

37. Rouzi AA, Sahly NN, Sahly NF, et al. Cisplatinum and docetaxel for ovarian cancer in pregnancy. Arch Gynecol Obstet. 2009;280:823–5.

38. Benjapibal M, Chaopotong P, Leelaphatanadit C, et al. Ruptured ovarian endodermal sinus tumor diagnosed during pregnancy: case report and review of the literature. J Obstet Gynaecol Res. 2010;36: 1137–41.

39. Barut A, Arikan I, Barut F, et al. Ovarian cancer during pregnancy. JPMA J Pak Med Assoc. 2011;61: 914–6.

40. Serkies K, Węgrzynowicz E, Jassem J. Paclitaxel and cisplatin chemotherapy for ovarian cancer during pregnancy: case report and review of the literature. Arch Gynecol Obstet. 2011;283(Suppl 1):97–100.

41. Viana LS, Tsunoda AT, Nunes JS, et al. Preservation of pregnancy in a patient with acute abdominal pain secondary to advanced and hemorrhagic yolk sac tumor of the right ovary. J Clin Oncol. 2011;29: e758-762.

42. Cardonick E, Bhat A, Gilmandyar D, et al. Maternal and fetal outcomes of taxane chemotherapy in breast and ovarian cancer during pregnancy: case series and review of the literature. Ann Oncol. 2012;23:3016–23.

43. Dobashi M, Isonishi S, Morikawa A, et al. Ovarian cancer complicated by pregnancy: analysis of 10 cases. Oncol Lett. 2012;3:577–80.

44. Ruiz Ramos J, Roma E, Palomar L, et al. Paclitaxel and carboplatin treatment for advanced ovarian cancer during pregnancy. Chemotherapy. 2013;59: 344–5.

45. Smith ER, Borowsky ME, Jain VD. Intraperitoneal chemotherapy in a pregnant woman with ovarian cancer. Obstet Gynecol. 2013;122:481–3.

46. Chen CH, Chiu LH, Chan C, et al. Management of ovarian cancer in 14th gestational week of pregnancy by robotic approach with preservation of the fetus. Gynecol Obstet Invest. 2015;80:139–44.

47. Hummeida ME, Hamad K, Gadir AF, et al. Ovarian cancer during pregnancy: a case report and literature review. Clin Pract. 2015;5:727.

48. Luh L, Mahendra I, Suwiyoga K, et al. Management comprehensive multidisciplinary of malignant ovarian germ cell tumors and feto—maternal outcome: a case series report and literature review. Open Access Maced J Med Sci. 2019;7:1174–9.

49. Moro F, Mascilini F, Pasciuto T, et al. Ultrasound features and clinical outcome of patients with malignant ovarian masses diagnosed during pregnancy: experience of a gynecological oncology ultrasound center. Int J Gynecol Cancer. 2019;29: 1182–94.

50. Xu T, Wang L, Jia Y, et al. Long-term multidisciplinary integrative therapy management resulted in favorable outcomes for ovarian cancer during pregnancy: a case report and literature review. J Ovarian Res. 2019;12:108.

51. Shim M, Mok C, Chang K, et al. Clinical characteristics and outcome of cancer diagnosed during pregnancy. Obstet Gynecol Sci. 2016;59:1–8.

52. Gasim T, Al Dakhiel S, Al Ghamdi A, et al. Ovarian tumors associated with pregnancy: a 20-year experience in a teaching hospital. Arch Gynecol Obstet. 2010;282:529–33.

53. Chang A, Patel S. Treatment of acute myeloid leukemia during pregnancy. Ann Pharmacother. 2015;49:48–68.

54. Cotteret C, Pham Y, Marcais A, et al. Maternal ABVD chemotherapy for Hodgkin lymphoma in a dichorionic diamniotic pregnancy: a case report. BMC Pregnancy Childbirth. 2020;20:231.

55. Frydenberg H, Harsem N, Ofigsbø Å, et al. Chemotherapy during pregnancy for advanced colon cancer: a case report. Clin Colorectal Cancer. 2020;19:141–4.

56. Loibl S, Han S, von Minckwitz G, et al. Treatment of breast cancer during pregnancy: an observational study. Lancet Oncol. 2012;13:887–96.

57. Maggen C, Lok C, Cardonick E, et al. Gastric cancer during pregnancy: a report on 13 cases and review of the literature with focus on chemotherapy during pregnancy. Acta Obstet Gynecol Scand. 2020;99:79–88.

58. Mandic A, Maricic S, Malenkovic G, et al. Neoadjuvant chemotherapy in locally advanced cervical cancer in pregnancy-Review of the literature. J BUON. 2020;25:597–604.

59. Mir O, Berrada N, Domont J, et al. Doxorubicin and ifosfamide for high-grade sarcoma during pregnancy. Cancer Chemother Pharmacol. 2012;69: 357–67.

60. Rivas G, Llinás N, Bonilla C, et al. Use of erlotinib throughout pregnancy: a case-report of a patient with metastatic lung adenocarcinoma. Lung cancer (Amsterdam, Netherlands). 2012;77:469–72.

61. Colombo N, Sessa C, du Bois A, et al. ESMO-ESGO consensus conference recommendations on ovarian cancer: pathology and molecular biology, early and advanced stages, borderline tumours and recurrent disease. Ann Oncol. 2019;30:672–705.

62. Torre LA, Trabert B, DeSantis CE, et al. Ovarian cancer statistics, 2018. CA Cancer J Clin. 2018;68: 284–96.

63. Uccello M, Boussios S, Samartzis EP, et al. Systemic anti-cancer treatment in malignant ovarian germ cell tumours (MOGCTs): current management and promising approaches. Ann Transl Med. 2020;8: 1713.

64. Frederiksen M, Casanova L, Schink J. An elevated maternal serum alpha-fetoprotein leading to the diagnosis of an immature teratoma. Int J Gynaecol Obstet. 1991;35:343–6.

65. Kim D, Park M. Maternal and fetal survival following surgery and chemotherapy of endodermal sinus tumor of the ovary during pregnancy: a case report. Obstet Gynecol. 1989;73:503–7.

66. Mantovani G, Gramignano G, Mais V, et al. Use of chemotherapy for ovarian cancer during human

pregnancy: case report and literature review. Eur J Obstet Gynecol Reprod Biol. 2007;131:238–9.

67. Metz S, Day T, Pursell S. Adjuvant chemotherapy in a pregnant patient with endodermal sinus tumor of the ovary. Gynecol Oncol. 1989;32:371–4.

68. Montz F, Horenstein J, Platt L, et al. The diagnosis of immature teratoma by maternal serum alpha-fetoprotein screening. Obstet Gynecol. 1989;73: 522–5.