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Research Article

Clinical Characteristics and Oncological Outcomes of Gynecological Cancer during Pregnancy: Ten-Year Hospital Experience

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Abstract

Objectives: To investigate the clinical characteristics and oncological outcomes of pregnant women concurrently diagnosed with gynecological cancer.

Methods: Medical records of pregnant patients diagnosed with gynecological cancer during January 2006 to September 2015 were retrospectively reviewed. Demographic data, tumor characteristics, treatment modalities, response rate, and survival duration were collected and analyzed.

Results: A total of 19 patients were diagnosed with gynecological malignancies during the study period. Of those, 12 patients had ovarian malignancies and 7 had cervical carcinoma. Of the 12 patients with ovarian malignancies, 6 had mucinous low malignant potential, 1 had serous carcinoma, 3 had immature teratoma, and 1 each had yolk sac tumor and dysgerminoma. Median gestational age (GA) at diagnosis was 16 weeks (interquartile range [IQR], 8.0 - 32.5). Delivery was occurred at median GA of 36 weeks (IQR, 8.3 - 38.0). All 12 patients had complete response, with no recurrence during a median follow-up of 42 months (IQR, 18.1 - 62.8). Of the 7 patients with cervical carcinoma, 4 had adenocarcinoma and 3 had squamous cell carcinoma. Cervical carcinoma was classified as stage IB1 in four patients, and IB2, IIB, and IIIB in one patient each. Mean age was 34.1 ± 6.5 years. Mean GA at diagnosis was 20.7 ± 7.7 weeks with median of 22 weeks (IQR, 14.0 - 28.0). Delivery was occurred at median GA of 37 weeks (IQR, 14.0 - 37.0). Finally, 5 patients were disease-free and two patients were alive with disease. Among those who received treatment, mean overall survival was 44.3 ± 32.1 months with median of 41.2 months (IQR, 13.1 - 77.8).

Conclusions: Favorable oncological outcomes were observed among the 19 patients diagnosed with ovarian or cervical cancer during pregnancy.

Keywords: *Thailand; Cervical Cancer; Ovarian Cancer; Pregnancy; Oncological Outcomes*

Abbreviations

95% CI: 95% Confidence Interval; A: Abortion; ACA: Adenocarcinoma; AWD: Alive with Disease; BEP: Bleomycin + Etoposide+ Cisplatin; BSO: Bilateral Salpingo-Oophorectomy; CCRT: Concurrent Chemoradiation; cC/S: Classical Cesarean Section; C/S: Cesarean Section; DFIU: Death Fetus in Utero; EOC: Epithelial Ovarian Cancer; ESGO: European Society of Gynaecological Oncology; FIGO: International Federation of Gynecology and Obstetrics; F/U: Follow-Up; G: Gravida; GA: Gestational Age; HR: Hazard Ratio; IQR: Interquartile Range; IR: Intermediate Pathological Risk; IUGR: Intra-Uterine Growth Retardation; LMP: Low Malignant Potential; MRI: Magnetic Resonance Imaging; N/A: Not Available Data; NAC: Neoadjuvant Chemotherapy; NED: No Evidence of Disease; NL: Normal Labor; OS: Overall Survival; P: Parity; PPCSS: Postpartum Complete Surgical Staging; RHPL: Radical Hysterectomy with Pelvic Lymphadenectomy; ‡RHPL+OT: Intrapartum Radical Hysterectomy with Pelvic Lymphadenectomy with Ovarian Transposition; RT: Radiation Therapy; SCCA: Squamous Cell Carcinoma; SD: Standard Deviation; SO: Salpingo-Oophorectomy; VEGF: Vascular Endothelial Growth Factor; V/E: Vacuum Extraction

Introduction

Cancer during pregnancy is defined as cancer diagnosed at any point during the first day of pregnancy to the end of the 1-year postpartum period time frame [1,2]. Management of cancer during pregnancy is challenging and requires a sophisticated approach so that both the mother and fetus can receive optimal treatment and care until the pregnancy reaches full term. The incidence of gynecological cancer during pregnancy was reported to be lower than the incidence of breast cancer, lymphoma, and melanoma during pregnancy. Cervical cancer during pregnancy was accounted for 1 - 12 per 10,000 pregnancies and is the third most common cancer in pregnancy [2-4]. Ovarian cancer is discovered in 1 per 100,000 pregnancies, and is the fifth most common cancer in pregnancy [2,5]. Given that more and more women are delaying pregnancy, it is likely that the incidence of these two types of gynecological cancer during pregnancy will rise. Data specific to gynecological cancer during pregnancy are scarce.

Purpose of the Study

The purposes of this study were to evaluate clinical characteristics, treatment modalities, short-term pregnancy outcome, and oncological outcomes of pregnant women who were diagnosed with concurrent gynecological cancer.

Materials and Methods

The protocol for this study was approved by the Siriraj Institutional Review Board, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand (COA no. 254/2017). The medical records of pregnant patients diagnosed with gynecological cancer at the Department of Obstetrics and Gynecology, Faculty of Medicine Siriraj Hospital during the January 2006 to September 2015 study period were retrospectively reviewed. Patient data through 30 June 2017 was included in our analysis. Demographic and obstetrics data, tumor characteristics, treatment modalities, response rate, and survival duration were collected, recorded, and analyzed. Data analysis was performed using SPSS Statistics version 18.0 (SPSS, Inc., Chicago, IL, USA). Evaluated variables were analyzed using descriptive statistics. Data are shown as number and percentage, mean ± standard deviation (SD), and/or median and interquartile range [IQR].

Results

A total of 19 pregnant patients were diagnosed with gynecological malignancies during the 10-year study period. Of those, 12 patients had ovarian malignancies and 7 had cervical carcinoma. Of the 12 patients were ovarian malignancies, 6 had mucinous low malignant potential (50%), 3 had immature teratoma (25%), 1 had yolk sac tumor (8.3%), 1 had dysgerminoma (8.3%), and 1 had serous carcinoma (8.3%) (Table 1). For disease staging, 10 women had stage I (83.4%), 1 had stage II (8.3%), and 1 had stage III (8.3%). Mean age was 31.2 ± 6.0 years, with a median of 31.5 years (IQR, 26 - 36). Mean gestational age (GA) at diagnosis was 19.5 ± 12.3 weeks, with a median of 16 weeks (IQR, 8.0 - 32.5). Mean GA at delivery was 27.5 ± 15.2 weeks, with a median of 36 weeks (IQR, 8.3 - 38.0). During pregnancy, 1 patient received 4 cycles of bleomycin, etoposide, and cisplatin combination regimen, and 1 patient was prescribed combined carboplatin and paclitaxel chemotherapy. All 12 ovarian malignancy patients had complete response, with no recurrence observed during a median follow-up duration of 42 months (IQR, 18.1 - 62.8).

Age (yr)	G, P, A	GA of diagnosis	Surgery	Histology	FIGO stages	GA of abortion/delivery and Route	Neonatal weight and Apgar score	Chemotherapy (* number of cycles)	Outcomes of mother/child	OS (mo)
23	2, 0, 1	13 wk	Right SO + Omentectomy	Yolk sac tumor	IC	36 wk, C/S	1,560 gm 9,10	BEP* 4 during pregnancy	NED/normal	36.4, loss F/U
25	1, 0, 0	34 wk DFIU	Left SO + Omentectomy	Dysgerminoma	IIIC	34 wk, NL	2,560 gm	BEP * 4 after delivery	NED/normal	3.9, loss F/U
29	1, 0, 0	19 wk	Left SO	Immature teratoma	IA	39 wk, C/S	3,265 gm 9,10	None	NED/normal	36.5
32	1, 0, 0	8 wk 6 d	Left SO + Omentectomy	Immature teratoma	IC	9 wk	-	BEP * 4 after induced abortion	NED	92.9
38	3, 1, 1	38 wk	Right SO + PP-CSS	Immature teratoma	IA	38 wk, C/S	2,800 gm 6,10	None	NED/normal	50.7
20	2, 0, 1	28 wk	Left SO	Mucinous LMP	IA	43 wk, NL	3,560 gm 10,10	None	NED/normal	25.4, loss F/U
31	2, 0, 1	4 wk 2 d	Right SO + Left S	Mucinous LMP	IA	5 wk Ectopic pregnancy	-	None	NED	67.1
31	2, 0, 1	13 wk 5 d	Left SO	Mucinous LMP	IA	38 wk 4 d, V/E	2,990 gm 8,10	None	NED/normal	46.7
36	2, 1, 0	8 wk	Right SO	Mucinous LMP	IA	10 wk abortion	-	None	NED	58.6
36	3, 1, 1	37 wk 2 d	Right SO	Mucinous LMP	IA	37 wk 2 d, C/S	2,880 gm 9,10	None	NED/normal	64.3
37	3, 1, 1	8 wk	BSO	Mucinous LMP	IB	9 wk abortion	-	None	NED	15.7, loss F/U
40	3, 2, 0	24 wk 5 d	BSO + Omentectomy	Serous EOC	IIC	36 wk 3 d, NL	2,320 gm 9,10	Carboplatin + Paclitaxel * 6 during pregnancy	NED/normal	6.0, loss F/U

Table 1 **:** *Characteristics and oncological outcomes of 12 patients who were diagnosed with ovarian malignancies during pregnancy.*

Abbreviations: A: Abortion; BEP: Bleomycin + Etoposide+ Cisplatin; BSO: Bilateral Salpingo-Oophorectomy; C/S: Cesarean Section; DFIU: Death Fetus in Utero; EOC: Epithelial Ovarian Cancer; FIGO: International Federation of Gynecology and Obstetrics; F/U: Follow-Up; G: Gravida; GA: Gestational Age; LMP: Low Malignant Potential; NED: No Evidence of Disease; NL: Normal Labor; OS: Overall Survival; P: Parity; PP-CSS: Postpartum Complete Surgical Staging; SO: Salpingo-Oophorectomy; V/E: Vacuum Extraction

Seven patients were diagnosed with cervical carcinoma was represent in table 2. Of those, 4 had adenocarcinoma and 3 had squamous cell carcinoma subtype. Cervical carcinoma staging according to International Federation of Gynecology and Obstetrics (FIGO) classification was stage IB1 in 4 patients, IB2 in 1 patient, IIB in 1 patient, and IIIB in 1 patient. Mean age was 34.1 ± 6.5 years, with a median of 35 years (IQR, 27.0 - 40.0). Mean GA at diagnosis was 20.7 ± 7.7 weeks, with a median of 22 weeks (IQR, 14.0 - 28.0). Delivery was occurred at mean GA of 30.1 ± 12.5 weeks, with a median of 37 weeks (IQR, 14.0 - 37.0). Five patients underwent classical cesarean section plus radical hysterectomy with pelvic lymphadenectomy and ovarian transposition, 1 patient received concurrent chemoradiation, and 1 patient refused treatment. At the end of the follow-up period, 5 patients were disease-free and 2 patients were alive with disease. Among those who received treatment, the mean overall survival was 44.3 ± 32.1 months, with a median of 41.2 months (IQR, 13.1 - 77.8). Recommendations for management of cervical carcinoma in pregnancy were summary and showed in table 3.

Age (yr)	G, P, A	GA of diagnosis	Histology	FIGO stages	NAC	Primary treatment	GA of abortion/ delivery and route	Neonatal weight (gm) and Apgar score	Adjuvant treatment	Outcomes of mother/child	OS (mo)
26	2, 1, 0	10 wk	SCCA	IIIB	-	Refused treatment	10 wk, induced abortion	-	-	N/A	Loss F/U
27	2, 1, 0	27 wk 2 d	ACA	IB1	None	‡RHPL+OT	37 wk 3 d, cC/S S	3,460 8,10	RT due to IR	†, AWD/normal	14.2, loss F/U
32	2, 1, 0	28 wk	ACA	IB1	None	‡RHPL+OT	39 wk, cC/S	3,240 10,10	None	NED/ normal	76.0
35	2, 1, 0	29 wk 1 d	ACA	IIIB	None	‡RHPL+OT	37 wk, cC/S	2,180 9,10	None	NED/ normal	61.9
35	1, 0, 0	15 wk 2 d	SCCA	IB1	None	‡RHPL+OT	37 wk 3 d, cC/S	2,370 9,10	None	NED/ normal	20.5
40	2, 1, 0	22 wk 6 d	ACA	IB1	None	‡RHPL+OT	37 wk, cC/S	3,000 9,10	None	NED/ normal	9.9, loss F/U
44	4, 2, 1	14 wk 4 d	SCCA	IIB	None	CCRT	15 wk, induced abortion	-	None	NED	83.2

Table 2: *Characteristics and oncological outcomes of 7 patients who were diagnosed with cervical cancer during pregnancy.*

Abbreviations: *A: Abortion; ACA: Adenocarcinoma; AWD: Alive with Disease; cC/S: Classical Cesarean Section; CCRT: Concurrent Chemoradiation; FIGO: International Federation of Gynecology and Obstetrics; F/U: Follow-Up; IR: Intermediate Pathological Risk; G: Gravida; GA: Gestational Age; N/A: Not Available Data; NAC: Neoadjuvant Chemotherapy; NED: No Evidence of Disease; OS: Overall Survival; P: Parity; RT: Radiation Therapy; SCCA: Squamous Cell Carcinoma; ‡RHPL+OT: Intrapartum Radical Hysterectomy with Pelvic Lymphadenectomy with Ovarian Transposition; †: Recurrence after Disease Free for 10 Months*

Discussion

When medical personnel are confronted with pregnant women with concurrent gynecological malignancies, issues that need to be considered include necessary special tests and safety, treatments options and potential adverse effects on the pregnancy, proper time to start treatment to optimize outcomes for both mother and fetus, delivery time and appropriate route, effect of treatment on breast feeding, and long-term surveillance of patients and children. A multidisciplinary approach is necessary to determine management methods and scheduling on a case-by-case basis. Optimal therapeutic management must include medical, ethical, psychological, religious, and legal conditions.

Ovarian cancer

The current study revealed the most common histology was low malignant potential (LMP) of mucinous ovarian tumor (50%), and the second common was germ cell tumors (41.7%). Most patients (83.3%) had stage I disease. Fifty percent of cases were diagnosed in the first trimester, and live birth occurred in 66.7% of patients. Only 16.7% of cases received adjuvant chemotherapy during pregnancy, with no observed adverse neonatal outcomes. These findings consistent with previous studies, which emphasize good prognostic feature of ovarian malignancies during pregnancy. In addition, most of the cases were achieved good pregnancy outcomes.

When compared with a systematic review of 105 epithelial ovarian cancer (EOC) in pregnancy, the authors stated that mean age was 31.6 ± 6.3 years. 63.8% of cases were classified in International Federation of Gynecology and Obstetrics (FIGO) stage I. The most common histology was serous carcinoma subtype, 47.6%. The most common GA at diagnosis was first trimester (45.3%), and the most common GA at delivery was third trimester (77.5%). A majority of those 105 cases had live birth (81.3%), of which 57% of mothers delivered full term. In-utero exposure to chemotherapeutic agents occurred in 21 of 105 patients (20%). After delivery, 43.8% of patients underwent secondary cytoreductive surgery. FIGO stage was an independent prognostic factor for 2-year survival with a hazard ratio (HR) of 44.6 [95% confidence interval (CI) 5.73 to 347, $P < 0.01$] for stage III, and a HR of 399 (95% CI 18.0 to 8812, $P > 0.05$) for stage IV disease [6].

A systematic review of 102 malignant ovarian germ cell tumors, reported mean age of 25.8±5.5 years. The most common histology was dysgerminoma, 38.2%. For staging, 76.4% of patients were classified as FIGO stage I. The most common GA at tumor surgery was second trimester (48%). A majority of cases had live birth (77.5%), with full-term delivery in 56.6% of cases. In-utero exposed to chemotherapeutic agents in proportion of 41.5%. The 5-year overall survival rate was 80.1%. FIGO stage II-IV was independent prognostic factor for 5-year survival with HR of 21.6 (95% CI 2.06 to 226, $P = 0.02$) [7]. Common histology was correlated with patients' age that is germ cell ovarian cancer usually occurs in younger age group. Discrepancy of histology type might be from regional or genetic diversity and small population in the current report. Prospective with large sample size and long term follow-up should be investigated.

Based on literatures review, routine antenatal ultrasonography detected adnexal tumor in proportion of 0.2 - 2% pregnancies with the vast majority are corpus luteum or theca lutein cysts, which normally disappear after the first trimester [5]. Emergency conditions, such as torsion or rupture, should be carefully observed for during expectant management. Adnexal torsion was found in 8% of cases, especially in cases with tumor size 6 - 8 cm and GA of 15 - 16 weeks [1]. Surgical intervention is usually performed at GA 14 - 18 weeks, which is pass over period of functional cyst and first trimester abortion [1,2,5]. In case of favored malignancies, surgery has to do right away due to rapid growing cancer in nature. Ovarian cancer predictive tools such as ultrasonography, Doppler study, serum tumor markers, or prediction scores were unreliable [8-11]. Many serum tumor markers are rising during normal pregnancy such as Cancer antigen 125 (CA-125), human chorionic gonadotropin, alpha-feto-protein, and squamous cell carcinoma antigen. Increasing of serum CA-125 level more than 35 IU/mL, or more than 65 IU/mL was found in 24%, and 16% of normal pregnancy, respectively. Return to baseline of CA-125 level happened at 2 - 4 weeks of postpartum period [12]. However, the levels of lactate dehydrogenase, human epididymis protein 4, inhibin B and anti-müllerian hormone, do not elevate in normal pregnancy but preeclampsia or some fetal anomalies or ovarian malignancies can produce these markers [5].

The most common ovarian cancer during pregnancy is non-epithelial tumors, 18 - 26% [7]. The least common are low malignant potential tumors and EOC [5]. 63.8% of ovarian cancers in pregnancy were classified as FIGO stage I, thus fertility preserving complete surgical staging should be considered [1,2,6]. Indications of adjuvant chemotherapy were similar as non-pregnant women; no benefit of chemotherapy in FIGO stage IA or IB, grade 1 diseases. Standard regimen for EOC is a combination of carboplatin with paclitaxel. Chemotherapy for non-EOC are triplets of cisplatin-vinblastine-bleomycin or cisplatin-etoposide-bleomycin [5,7] or alternative regimen of carboplatin combined with paclitaxel [1,5]. Neoadjuvant chemotherapy (NAC) is treatment of choice for advanced stage EOC and reoperation has to be performed for optimal cytoreductive surgery after delivery [1,2,5,6,12]. Chemotherapeutic agents can induce embryonic death or abortion if used in first two weeks of gestation, and caused major congenital malformations in the first eight weeks of gestation [13]. Carboplatin and paclitaxel data in pregnancy is safe to be given at second or third trimesters of pregnancy. Bleomycin in pregnancy has been associated with intra-uterine growth retardation (IUGR) and preeclampsia. Secondary leukemia from etoposide has been reported [5]. Gemcitabine is related to IUGR. Other agents such as 5-fluorouracil, anthracyclines, cyclophosphamide, vinca alkaloids, were also safe. Anti-vascular endothelial growth factor (VEGF) antibody inhibits organogenesis and induced early pregnancy [14,15]. Pregnancy status increases plasma volume, extracellular fluid, distribution volume, glomerular filtration, and fat mass. However, the same dose and schedule as non-pregnancy was recommended. Chemotherapy should not administer in first trimester because of the risk of malformation between 10 - 20% and this risk will decrease to 1.3% in the third trimester. The last chemotherapy cycle should be administered at least 3 weeks before delivery, to avoid nadir of maternal and neonatal myelosuppression and avoid accumulation of chemotherapy in fetus [5]. Granulocyte-colony stimulating factor can cross placenta, limited data in pregnancy and does not seem to cause any significant sequelae. Ondansetron and metoclopramide are safe. Erythropoietin does not cross placenta, can be used in the selected cases [2].

Postdelivery management, re-staging operation should be considered for apparently early stages of EOC [12,16]. For germ cell tumors, surgery should be completed after finishing childbearing [17]. Posttreatment surveillance is included history taking, clinical evaluation, tumor markers in case of initially elevated, and further investigations only if clinical suspicion [18]. Genetics testing should be considered in case of EOC, especially if present in this age group [19].

Cervical cancer

The current study revealed that the proportion of adenocarcinoma subtype (57.1%) was higher than squamous cell carcinoma. Most of them were classified as FIGO stage IB1 (57.1%). The median age was younger than non-pregnant women with cervical carcinoma, 35 years. All of them were diagnosed during second trimester of gestation. A case control study of 28 pregnant women diagnosed with cervical cancer and matched with 52 non-pregnant cases by same stage and age, most of them were stage IB1. The mean GA at diagnosis of cervical cancer was 17.4 weeks. 25% of patients were pregnancy termination before start of definite treatment. Mean GA at delivery was 36.1 weeks. When compared with non-pregnant patients, time to treatment was significant longer in pregnant patients, 20.8 vs 7.9 weeks, P = 0.0014. For 3.4 and 3.7 years of follow-up period, the survival of pregnant patients were similar to non-pregnant patients, 89.3% vs 95.2%, P = 0.08 [3].

Clinical staging for cervical cancer was recommended by FIGO committee. Colposcopy and biopsies by experience hand, diagnostic conization by shallow loop electrosurgical excision procedure in case of suspicious invasion is reasonable. Limit the exposure to ionizing radiation imaging studies, so chest X-ray with abdominal shield and magnetic resonance imaging (MRI) without gadolinium in selected cases should be strongly considered [1,2]. 70% of cervical cancer in pregnancy were classified as stage I [12]. Main treatment in cervical cancer with either radical surgery or concurrent chemoradiation can cause fetal death or pregnancy termination and will be definitely deprived of future fertility after treatment. The main considerations of treatment plan are (i) FIGO stages, (ii) histological subtype, and (iii) pregnancy status such as gestational age, fetal well-being, maternal diseases, and couple desired of pregnancy preservation. If there is no desire to continue pregnancy, radiation therapy or radical surgery with fetus in utero can be performed immediately as in non-pregnant patients. The radiation dose of 34 - 40 Gy would induce spontaneous abortion.

Management in case of desired to preserve pregnancy is remaining experimental. In the past, diagnosis of cervical cancer during first or second trimester should receive treatment without delay. In cases where diagnosis was done in third trimester, treatment can be postponed to after delivery. In the era of MRI and laparoscopy, the role of lymph node evaluation to classify pregnant patients into low or high risk of disease metastasis, and to metastatic survey during delayed definite treatment. Obstetricians have technology of fetal monitoring during lymphadenectomy or chemotherapy treatment or delayed treatment. Through this technology, delayed definite primary treatment until fetal maturity is another choice.

All health organizations recommended similar management for stage IA1 and stage IB2 to IVB patients. For stage IA1, treatment should be delayed until fetal maturation. Patients with stage IB2 to IVB patients should receive urgent treatment, for the best care of mother. The management of stage IA2 to IB1 cervical cancer in pregnancy preserving is controversial and should be discussed on a case-by-case basis.

In cases where a pregnancy is being preserved and the patient has stage IA2 and small IB1 (1) or small IB1 (20) should have pathology evaluation of nodal metastasis. If no nodal metastasis, treatment should be postponed at or after delivery. Laparoscopic pelvic lymphadenectomy is possible and safe between GA 13-22 weeks with 5 strategic considerations (i) left lateral tilt position in GA ≥ 20 weeks, (ii) open Hassan technique, (iii) intra-abdominal pressure of 10 - 13 mmHg, (iv) a maximum operating time of 90 minutes, (v) expert surgeons. If nodal metastasis is present, NAC during pregnancy was suggested. The regimens recommendation were cisplatin 50 - 100 mg/m2, usually 75 mg/m2 every 3 weeks interval or weekly cisplatin 20 - 50 mg/m2 or carboplatin AUC 5 - 7.5 every 3 weeks and paclitaxel 175 mg/m2 every 3 weeks [1,2]. A delay of treatment for 8 weeks for tumor size > 4 cm is reasonable and does not seem to have a major impact on survival [20]. The European Society of Gynaecological Oncology (ESGO) stated that no recurrent was detected in stage IB1 patients who had median time of treatment delayed for 16 weeks with survival of 95% at means follow-up time of 37.5 months [1]. In cases of diagnosed after 22 - 25 weeks gestation, laparoscopic lymphadenectomy is not possible, so the authors recommended delay of treatment until fetal maturity for stage IA1 and smaller IB1, and NAC for higher stages [1].

Some authority suggested treatment for IA1 can be delayed until delivery. Disease stage IA2 to smaller than 2 cm of stage IB1, should be manage according to gestational age of abortion criterion. If cancer was diagnosed before 22 - 25 gestational weeks, laparoscopic lymphadenectomy is useful to determine high risk for distant metastasis patients. In case of cancer diagnosed when gestation more than 22 - 25 weeks, an intentional delay of treatment until fetal maturity is an option. If disease was classified as stage IB1 > 2 cm to stage IVB, chemotherapy should be prescribed in the second and third trimesters of gestation during delayed concurrent chemoradiotherapy for fetal maturation. Chemotherapy should be stopped 3 weeks before delivery; generally stopped before 35 gestational weeks [1].

Due to episiotomy recurrence, cesarean section was recommended, but in the case where it is clear from tumor, vaginal delivery is an option. Posttreatment surveillance schedule interval is similar to ovarian cancer and vaginal cytology should be collected every year [18]. Due to increasing of maternal age and low proportion of screening coverage in Thailand, prenatal or first visit of antenatal care should provide cervical cancer screening. Meticulous pelvic examination in pregnant women who had vaginal bleeding should be done.

References	Recommendations
French 2009	1. Cervical cancer diagnosed after fetal maturation (fetal maturity is attained between GA 26 to 30 weeks): preservation of the fetus and delivery by cesarean section with nodal staging or RHPL, simultaneously. 2. Cancer diagnosis before fetal maturation and exclusion of aggressive histology: 2.1 Stage IB1 at GA 18 to 22 weeks (laparoscopy is feasible) 1.1.1 Smaller IB1 (<2 cm): laparoscopic pelvic lymphadenectomy • absence of nodal involvement: continue pregnancy with clinical assessment and MRI every 4 to 8 weeks, and RHPL during cesarean section • presence of nodal involvement: pregnancy interruption and CCRT + para-aortic nodes evaluation (by laparoscopic para-aortic nodes dissection or Positron Emission Tomography - Computed Tomography) 2.1.2 IB1 (size 2 to 4 cm): pregnancy termination and initiation of standard treatment 2.2 Stage IB1 diagnosed after GA 22 weeks 2.2.1 smaller IB1 (<2 cm): pregnancy continuation with clinical assessment and MRI every 4 to 8 weeks, and RHPL during cesarean section 2.2.2 IB1 (size 2 to 4 cm): individual discussion. NAC is an option for tumor size close to 4 cm 2.3 Higher stage diagnosed before GA 22 weeks: CCRT right away after pregnancy termination or with fetus in situ. NAC during intentional delayed of treatment for fetal maturity. 2.4 Higher stage diagnosed after GA 22 weeks: CCRT following cesarean section, after fetal maturity has been attained and should not delay treatment more than 8 weeks. NAC is an option for intentional delay in this situation. 3. Cancer diagnosed during the first or second trimester with aggressive histology: definite treatment without delay.
ESGO 2014	1. Stage IA1, conization alone during pregnancy is safe. 2. If cancer is diagnosed before 22-25 gestational weeks, laparoscopic lymphadenectomy is useful to determined high risk for distant metastasis. 2.1 Disease stage IA2 to smaller IB1 (<2 cm); □ absence of nodal involvement: (i) pregnancy continuation with clinical assessment and MRI every 4 to 8 weeks, and RHPL during cesarean section after fetal maturity (ii) simple trachelectomy during pregnancy is optional. □ presence of nodal involvement: Pregnancy termination and initiation of standard treatment 2.2 Stage IB1, larger than 2 cm □ absence of nodal involvement: NAC until fetal maturity □ presence of nodal involvement: Pregnancy termination and initiate standard treatment □ or NAC whether laparoscopic lymphadenectomy or not 3. Stage IB2 and higher stages □ NAC until fetal maturity □ Therapeutic value of pelvic staging lymphadenectomy before start chemotherapy is controversy. 3. In case of cancer diagnosed at more than 22-25 weeks of gestation, laparoscopic lymphadenectomy is not feasible. 3.1 Disease stage IA2 to smaller IB1 (<2 cm); delay of treatment until fetal maturity 3.2 Higher stages, NAC is the only way to preserve pregnancy.

Table 3: *Recommendations for management of cervical cancer in pregnancy [1,20].*

Abbreviations: *CCRT: Concurrent Chemoradiation; GA: Gestational Age; MRI: Magnetic Resonance Imaging; NAC: Neoadjuvant Chemotherapy; RHPL: Radical Hysterectomy with Pelvic Lymphadenectomy*

This study has some mentionable limitations. First and consistent with the retrospective nature of this study, some patient data may have been missing or incomplete. Second, given the relative rarity of gynecological cancer in pregnancy, the size of the study population was relatively small. Third, the patients enrolled in this study were from a single center. Moreover, our center is Thailand's largest tertiary referral hospital, which means that we are often referred patients with complicated and intransigent conditions. As such, it is possible that our findings may not be generalizable to patients with the same condition in other settings. Further study in hormonal status after ovarian transposition, in gynecological cancer diagnosed in the first postpartum year, and in the long-term data of the children born to these women is needed.

Conclusion

Twelve ovarian cancer and 7 cervical cancer patients were diagnosed during pregnancy, had favorable oncological outcomes. Based on the current data and update in literature, pregnancies complicates with gynecological cancer remains as understudied and infrequent. A team of experts is essential/mandatory in treatment for this pregnancy complication. Purpose of care is definite treatment without delayed and full-term pregnancy should be always. Pregnancy does not deteriorate the oncological outcomes of cervical or ovarian cancers, when balanced with stage of diseases. Chemotherapy is safe for second and third trimester period. Delivery mode should be based on obstetrics indications. Placenta and child should be carefully evaluated for micrometastasis. When compared by stage, survival rates for pregnancy patients with cervical or ovarian cancers are comparable to those non-pregnant patients. It is necessary to establish more in aspect of pathophysiology, spreading pattern, aggressiveness, appropriate treatment protocol, and knowledge transmission to optimize the best therapeutic outcomes. Long term outcomes of children should be explored in physical, functional and cognitive development.

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Conflict of Interest Declaration

All authors declare no personal or professional conflicts of interest, and no financial support from the companies that produce and/or distribute the drugs described in this report.

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