Cervical Cancer in Pregnancy

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ABSTRACT

Carcinoma of the uterine cervix is one of the most common malignant neoplasms among women and remains the leading female malignancy in Thai women. Cervical cancer diagnosed during pregnancy remains a therapeutic challenge for physicians. Pregnant women should have cervical cytology screening at their first prenatal visit. In cases of cytological abnormality, colposcopy is indicated. Cervical conization is used for the diagnostic role only. The management of invasive cancer depends on the gestational age at diagnosis, stage of disease, patient's desire of pregnancy, ethics and religious belief s including family and decision making by multidisciplinary teams.

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Approximately 500,000 new cases of invasive cervical cancer have been diagnosed worldwide each year with more than 250,000 women dying of the disease. Cervical cancer is the second most common cancer in women after breast cancer. In Thailand, it is the most frequent cause of cancer in women, with more than 6,000 new cases diagnosed and nearly 3,200 dying from this disease each year.[1] In developed countries, the incidence and mortality have declined over the past 50 years due to the increased availability of cervical cancer screening programs.[2] However, cervical cancer remains a leading cause of cancer deaths among women with a low socioeconomic level.

The mean age at diagnosis for invasive cervical cancer is 52.2 years, while the distribution of cases is bimodal, with peaks at 35-39 years and 60-64 years.[3] This age distribution is indicative of the significant proportion of women diagnosed with cervical cancer in the reproductive-age group, with one-third of cases occurring in women age 35 years or younger.[4] As women continue to delay childbearing, the frequency of cervical cancer during pregnancy will likely increase. It is estimated that 1 to 3 percent of women diagnosed with cervical cancer are pregnant or postpartum at the time of diagnosis.[5,6] Cervical cancer is one of the most common malignancies in pregnancy, with a reported incidence of 0.8 to 1.5 cases per 10,000 births, depending on the inclusive postpartum interval.[7-10] For practical purposes, cases of cervical cancer diagnosed within 6 months of an antecedent pregnancy should be considered to have been coexistent with pregnancy. About one-half of these cases are diagnosed prenatally and the other half are diagnosed within 12 months of delivery.[8] It is therefore important for clinicians caring for women in the reproductive-age group to be familiar with the diagnosis and management of a pregnant woman with cervical cancer.

During the past decade, epidemiologic evidence has accumulated, implicating infection with high-risk types of genital human papillomavirus (HPV) as a necessary cause of squamous cell carcinoma the cervix and related precursor lesions.[11,12] Previous studies have indicated a proportionately higher frequency of cervical HPV infection in pregnant women compared with the expected frequency in non-pregnant controls.[13,14] The down-regulation of cell-mediated immunity during pregnancy and pregnancy-related active metaplasia of the cervical epithelium are likely contributing factors to these observations.[15-17]

Cytologic screening

The concept of utilizing exfoliative cytology to identify women with invasive cervical cancer was introduced by Papanicolaou and Babes in the 1920s.[18] Pap smear has proven to be the most efficacious and cost-effective method of cancer screening. In the 1960s, cervical cytology began to be widely used in many developed countries as a technique for cervical cancer prevention and has decreased both the incidence and mortality from cervical cancer.[2,19] With the incorporation of cervical cytology into routine prenatal screening, clinicians are frequently presented with management decisions regarding cervical abnormalities during pregnancy.

In general, 1.3% to 2.2% of pregnant women will have cervical cytologic abnormalities detected during pregnancy, although the exact incidence is highly dependent on the population screened and the referral base of the reporting institution.[20,21] Pregnant women should receive cervical cytology screening at their first prenatal visit and samples should be collected from both the ectocervix and the endocervical canal.

Abnormal cytology and management

All women with a cytologic cervical abnormality

during pregnancy should undergo colposcopic examination. Colposcopically directed biopsy is both safe and efficacious when performed during pregnancy. The diagnostic accuracy approaches that of cervical conization, with fewer complications.[22-25] While biopsy of colposcopic abnormalities can be performed during all trimesters of pregnancy, many clinicians will defer biopsy until the second trimester when the risk of incidental spontaneous pregnancy loss is minimal. The risk of bleeding and premature rupture of membranes generally precludes the use of endocervical curettage during pregnancy.[26]

A biopsy-confirmed low-grade squamous intraepithelial lesion (LSIL) can be followed safely through pregnancy without risk of progression to invasive cancer.[27,28] These patients should have cervical cytology performed during each trimester and be reevaluated 8 to 12 weeks postpartum for definitive management, if necessary. For women with a high-grade squamous intraepithelial lesion (HSIL), close cytologic and colposcopic surveillance is indicated every 8 to 12 weeks, with additional biopsies if there is suspicion of disease progression. With adequate surveillance and assurance that early invasive disease is not present, definitive therapy should be deferred until after delivery. Because of the possibility of spontaneous regression, all patients should be reevaluated with colposcopy and biopsy 8 to 12 weeks postpartum prior to the initiation of definitive treatment.

Cervical conization

Cervical conization offers excellent diagnostic accuracy, however, it has a significant complication rate, when it is performed during pregnancy. The increased uterine and cervical vascularity associated with pregnancy makes hemorrhage a significant risk from conization performed during pregnancy.[29] The risk of excessive blood loss (exceeding 500 ml) is related to the trimester of pregnancy in which the conization is performed, ranging from negligible risk during the first trimester, to 5% in the second trimester, and 10% in the third trimester.[30] Traditional indications for this procedure in the non-pregnant state are not directly applicable to the obstetric population. For obstetric patients, conization is indicated in the presence of microinvasion on a colposcopically directed biopsy or persistent cytology evidence of invasive carcinoma in the absence of colposcopic confirmation.

Spontaneous pregnancy loss follows cervical conization in 3.6% to 8.1% of patients, although the risk is highest if conization is performed in the first trimester (17.7%).[31-33] Consequently, conization should be avoided in the first trimester. The optimal time for cervical cone biopsy is between 14 and 20 weeks' gestational age. Conization should not be attempted within 4 weeks of the anticipated delivery date because of the potential risk of cervical laceration and excessive bleeding.

Symptoms

The diagnosis of cervical cancer is often delayed in pregnant women since many of these symptoms are similar to those associated with a normal pregnancy. In one study, the average duration of symptoms before diagnosis of cervical cancer in pregnancy was 4.5 months.[29] In younger pregnant women, the suspicion for malignancy is usually low, and diagnosis delays are especially common. Vaginal bleeding is the most common presenting complaint in obstetric or postpartum patients with cervical cancer, followed by a vaginal discharge which may be interpreted as a normal physiologic change during pregnancy. The presenting symptoms of cervical cancer in pregnancy are dependent upon the clinical stage and lesion size. In two series, all pregnant patients with stage IA and 50 percent of those with stage IB carcinoma were asymptomatic at the time of diagnosis.[8,34] Patients with symptomatic stage IB disease presented with abnormal vaginal bleeding or discharge. Clinical manifestations in patients with more advanced disease also included pelvic pain, sciatica-type leg pain, flank pain, chronic anemia, and shortness of breath. Any pregnant women presenting with symptomatic vaginal bleeding or discharge should be completely evaluated with pelvic examination and cytology.

Staging

Most patients are diagnosed at an early stage of disease.[35,36] This is probably a result of routine prenatal screening, but it is also possible that advanced stage disease interferes with conception. The International Federation of Gynecology and Obstetrics (FIGO) staging system for the diagnosis and evaluation of cervical cancer is based on clinical evaluation (inspection, palpation, colposcopy), histologic examination of directed biopsy or conization specimens and radiographic examination of the chest, kidneys, and skeleton (Table 1).

A review of previous published literature found that the stage distribution for pregnant women with cervical cancer was not significantly different from the stage distribution for non-pregnant counterparts.[37] However, more recent series have found that the majority of patients with cervical cancer during pregnancy have stage I disease, with approximately 76% being stage IB.[8,38-40] This favorable stage distribution of cervical cancer during pregnancy is likely related to both the incorporation of screening cytology into prenatal care and the association of early-stage disease with younger age.[4,35,36]

Effect of pregnancy, gestation age at diagnosis, and mode of delivery on survival

The physiologic immunosuppressant during pregnancy has generated concern that the gravid state may have an adverse effect on the overall prognosis of concomitant invasive cervical cancer. Fortunately, studies controlling the clinical stage of disease at diagnosis and other confounding variables have not confirmed this hypothesis.[36,39,41,42] Studies comparing women with pregnancy-associated cervical cancer and control women matched for age, stage, tumor type, and treatment modality by Zemlickis et al[36] and Van der Vange et al[42] showed no difference in survival between patients diagnosed during pregnancy and non-pregnant controls. The authors concluded that pregnancy has no adverse effect on the prognosis of cervical cancer. Other investigators have also confirmed that overall pregnancy does not have an adverse effect on the survival of patients with cervical cancer.[39,41]

For pregnant patients with early-stage cervical cancer (stage I or II), gestation age at the time of diagnosis has no effect on survival, with 5-year survival

TABLE 1. FIGO clinical staging and classification of cancer of the cervix.

Stage		Description
0		Carcinoma in situ, intraepithelial carcinoma; case of stage 0 should not be included in any therapeutic statistics for invasive carcinoma.
I		The carcinoma is strictly confined to the cervix (extension to the corpus should be disregarded).
IA		Invasive cancer identified only microscopically. All gross lesions, even with superficial invasion are stage IB cancers. Invasion is limited to measured stromal invasion with a maximum depth of 5 mm taken from the base of epithelium, either surface or glandular from which it originated. Vascular space involvement, either venous or lymphatic should not be alter the staging.
	IA1	Measured invasion of stroma no greater than 3 mm in depth and no wider than 7 mm.
	IA2	Measured invasion of stroma greater than 3 mm and no greater than 5 mm in depth and no wider than 7 mm.
IB		Clinically visible lesions confined to the cervix or preclinical lesions greater than stage IA.
	IB1	Clinical lesion no greater than 4 cm in size.
	IB2	Clinical lesion greater than 4 cm in size.
II		The carcinoma extends beyond the cervix, but has not extended on to the pelvic wall; the carcinoma involves the vagina but not as far as the lower third.
	IIA	No obvious perametrial involvement.
	IIB	With parametrial involvement.
III		The carcinoma has extended on to the pelvic wall; on rectal examination there is no cancer free space between the tumor and the pelvic wall; the tumor involves the lower third of the vagina; all cases with the hydronephrosis or non-functioning kidney should be included, unless they are known to be due to other causes.
	IIIA	No extension on to the pelvic wall, but involvement of the lower third of the vagina.
	IIIB	Extension onto the pelvic wall or hydronephrosis or non-functioning kidney.
IV		The carcinoma has extended beyond the true pelvis or has clinically involved the mucosa of the bladder or rectum.
	IVA	Spread of the growth to adjacent organs.
	IVB	Spread to distance organs.

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rates ranging from 70%-90%.[39] Cervical cancer presenting during the third trimester or postpartum is frequently associated with a delay in diagnosis, because of confusion between symptoms of cervical cancer and those of normal pregnancy. After controlling for the clinical stage, no independent adverse effect on survival can be demonstrated for the trimester of diagnosis.[36]

The optimal method of delivery for women with cervical cancer associated with pregnancy is still controversial. Retrospective reviews have shown no association between the route of delivery and maternal survival in women with early-stage cervical cancer. Among patients with advanced disease (stage III or IV) equivalent survival rates can be expected for vaginal and abdominal delivery after controlling for tumor volume.[34] Because large tumor mass poses a risk for both pelvic outlet obstruction and significant hemorrhage during labor, abdominal delivery is recommended for pregnant patients with advanced cervical cancer.

Treatment

There are no data from large randomized trials upon which to base recommendations for the care of pregnant patients with cervical cancer. Therefore, management is based upon evidence from randomized trials in non-pregnant women, findings from observational studies of pregnant women, and the unique medical and ethical considerations underlying each individual case. Once the diagnosis of cervical cancer has been established, individual treatment recommendations are dependent on the stage of disease, gestational age at the time of diagnosis, the desires of the mother regarding continuation of the pregnancy, and the risks of modifying or delaying therapy during pregnancy.

Microinvasive carcinoma

The diagnosis of microinvasive carcinoma of the cervix (stages IA1 or IA2) can only be reliably established by histologic examination of a sufficiently large, intact biopsy specimen (conization) with clear surgical margins. There is no convincing evidence that the route of delivery influences the outcome for patients with microinvasive carcinoma. Vaginal delivery can usually be accomplished and abdominal delivery should generally be dictated by obstetric indications and definitive therapy delayed until 4 to 6 weeks after delivery. For well documented stage IA1 lesions, conization alone is adequate treatment. Total hysterectomy may be performed if the patient has completed her child-bearing. Patients with stage IA2 lesions should be treated with a modified radical hysterectomy with pelvic lymphadenectomy or radiation therapy. If cesarean delivery is required for obstetric reasons or the patient desires immediate treatment, surgical therapy can be rendered concurrent with abdominal delivery.

Stage IB to IIA

For a pregnant patient with stage IB or IIA disease, both radical surgery and radiation therapy offer similar cure rates.[29,43] Definitive surgery for stage IB or IIA disease consists of radical hysterectomy with bilateral pelvic lymphadenectomy. Advantages of the

surgical approach include the provision of immediate treatment of the pelvic tumor, as well as the opportunity to perform a through pelvic and abdominal exploration. Patients can then be offered an individualized treatment plan based on their precise disease status. In young, reproductive-age patients, surgery permits conservation of the ovaries and allows preservation of vaginal anatomy. Surgical therapy in pregnancy is feasible and safe, with acceptable associated morbidity. Surgical tumor clearance and lymph node yield are comparable to radical hysterectomy performed in non-pregnant patients. If the decision is made to proceed with therapy prior to 20 weeks gestation, radical hysterectomy is performed with the fetus in situ. After 20 weeks, the uterus should be evacuated prior to hysterectomy.

Patients with stage IB or IIA lesions who are poor operative candidates may be treated by primary radiation. The primary advantage of radiation therapy is that it can be used with curative intent for all stages of disease and for most patients regardless of age, body habitus, or coexistent medical conditions. Ovarian function is lost in all patients undergoing therapeutic doses of radiation to the pelvis. Radiation therapy may also be complicated by vaginal fibrosis and associated sexual dysfunction.

Stage IIB to IV

Primary irradiation is the standard therapeutic approach for patients with stage IIB or greater cervical cancer. Concurrent chemo-radiation therapy with a platinum-based regimen should be considered. Radiation therapy for stage IIB to IV carcinoma of the cervix should be initiated as soon as possible in the presence of advanced disease. If the diagnosis is made in the first or second trimester, treatment is initiated with the fetus in situ. Spontaneous termination of the pregnancy will need to occur prior to the administration of 4,000 cGy of external-beam radiation. Spontaneous abortion will occur an average of 33 days after beginning external beam irradiation during the first trimester, while a mean of 44 days is required during the second trimester.[44] If the diagnosis is made in the third trimester, fetal viability is assessed and delivery accomplished by cesarean section with a vertical uterine incision. Therapeutic radiation is then instituted by the second and third postpartum week. Patients with advanced metastatic disease (stage IVB) are usually treated with chemotherapy alone or in conjunction with palliative radiation therapy. These patients have a uniformly poor prognosis regardless of treatment modality.

Treatment delays

In the case of a desired but immature pregnancy, the question of delayed therapeutic intervention will undoubtedly arise. The literature examining therapeutic delays of cervical cancer treatment during pregnancy consists largely of small case series of selected patients with early-stage disease.[34,40,45] Considering the majority of these reports, it appears that modest therapeutic delays in patients with early invasive carcinoma of the cervix are not detrimental to maternal outcome and can result in significant fetal salvage. However, the acceptable duration of delay is not entirely clear and should be dependent on the clinical stage, gestational age at diagnosis and histopathologic features. Stage IA1 tumors diagnosed by an adequate conization specimen may be managed expectantly during all trimesters until after delivery, at which time the patient is reevaluated. Patients with stage IA2 disease diagnosed during the third trimester may delay therapy until fetal viability is achieved. Patients with these histologic features diagnosed during the first or second trimesters may consider either immediate treatment or therapeutic delay, depending on the patient's wishes. Therapeutic delay for these patients may carry some additional risk of disease progression; however, the degree of that risk is uncertain. Close clinical surveillance is mandatory if treatment is deferred until after delivery.

For patients diagnosed with stage IB1 tumors during the second or third trimester, a delay in instituting therapy to improve fetal outcome is also a reasonable option based on the available limited data. In the absence of substantial objective data, limiting the interval between diagnosis and therapeutic intervention to no more than 12 weeks seems prudent for these patients. There is probably a greater risk of disease progression associated with delayed therapy for patients with large-volume disease (stage IB2 and higher). In these patients, therapy should probably not be deferred for more than 6 weeks after diagnosis in order to maximize the chances for maternal survival. Patients choosing to delay therapy should be monitored closely for evidence of disease progression, with clinical evaluation performed by an experienced examiner at 2- to 4-week intervals until delivery. Neonatal outcome is closely linked to gestational age at the time of delivery. Therapy should only be delayed until there is documented fetal lung maturity. It is reasonable to perform amniocentesis for lung maturity assessment beginning at approximately 30 to 31 weeks. In addition, dexamethasone can be used to hasten the development of fetal lung maturity.

Follow-up

Since approximately 80% of recurrences will present within 2 years of definitive therapy; patients should have a complete physical and pelvic examination every 3 months for 2 years after treatment for cervical cancer, and then examination should be done every 6 months for an additional 3 years. Vaginal and cervical cytology should be performed at each visit.

SUMMARY

Management of cervical intraepithelial neoplasia (CIN) during pregnancy consists of almost exclusively expectant observation, with definitive therapy deferred until after delivery. Conization is reserved for rare cases in which microinvasive carcinoma is suspected or the diagnosis of invasive carcinoma will result in a change in the timing or route of delivery. Survival rates for pregnant patients with cervical cancer are comparable to those for non-pregnant women, when compared by stage. Furthermore, delays in therapy in order to improve fetal salvage rates appear safe in selected circumstances for early-stage disease. However, such delays in therapy should only be undertaken with the fully informed consent of patients, and treatment should not be postponed beyond the time that fetal viability is reached.

REFERENCES

1. Parkin DM, Bray F, Ferlay J, Pisani P. Global cancer statistics, 2002. CA Cancer J Clin. 2005 Mar-Apr;55(2):74-108.
2. Nieminen P, Kallio M, Hakama M. The effect of mass screening on incidence and mortality of squamous and adenocarcinoma of cervix uteri. Obstet Gynecol. 1995 Jun;85(6):1017-21.
3. Jemal A, Thomas A, Murray T, Thun M. Cancer statistics, 2002. CA Cancer J Clin. 2002 Jan-Feb;52(1):23-47.
4. Clark MA, Naahas W, Markert RJ, Dodson MG. Cervical cancer: women aged 35 and younger compared to women aged 36 and older. Am J Clin Oncol. 1991 Aug;14(4):352-6.
5. Nguyen C, Montz FJ, Bristow RE. Management of stage I cervical cancer in pregnancy. Obstet Gynecol Surv. 2000 Oct;55(10):633-43.
6. Creasman WT. Cancer and pregnancy. Ann N Y Acad Sci. 2001 Sep; 943:281-6.
7. Demeter A, Sziller I, Csapo Z, Szantho A, Papp Z. Outcome of pregnancies after cold-knife conization of the uterine cervix during pregnancy. Eur J Gynaecol Oncol. 2002;23(3):207-10.
8. Duggan B, Muderspach LI, Roman LD, Curtin JP, d'Ablaing G, 3rd, Morrow CP. Cervical cancer in pregnancy: reporting on planned delay in therapy. Obstet Gynecol. 1993 Oct;82(4 Pt 1):598-602.
9. Smith LH, Dalrymple JL, Leiserowitz GS, Danielsen B, Gilbert WM. Obstetrical deliveries associated with maternal malignancy in California, 1992 through 1997. Am J Obstet Gynecol. 2001 Jun;184(7):1504-12; discussion 12-3.
10. Smith LH, Danielsen B, Allen ME, Cress R. Cancer associated with obstetric delivery: results of linkage with the California cancer registry. Am J Obstet Gynecol. 2003 Oct;189(4):1128-35.
11. Bosch FX, de Sanjose S. Chapter 1: Human papillomavirus and cervical cancer--burden and assessment of causality. J Natl Cancer Inst Monogr. 2003;(31):3-13.
12. Walboomers JM, Jacobs MV, Manos MM, Bosch FX, Kummer JA, Shah KV, et al. Human papillomavirus is a necessary cause of invasive cervical cancer worldwide. J Pathol. 1999 Sep;189(1):12-9.
13. Fife KH, Katz BP, Roush J, Handy VD, Brown DR, Hansell R. Cancer-associated human papillomavirus types are selectively increased in the cervix of women in the first trimester of pregnancy. Am J Obstet Gynecol. 1996 May;174(5):1487-93.
14. Schneider A, Hotz M, Gissmann L. Increased prevalence of human papillomaviruses in the lower genital tract of pregnant women. Int J Cancer. 1987 Aug 15;40(2):198-201.
15. Gall SA. Maternal adjustments in the immune system in normal pregnancy. Clin Obstet Gynecol. 1983 Sep;26(3):521-36.
16. Weinberg ED. Pregnancy-associated depression of cell-mediated immunity. Rev Infect Dis. 1984 Nov-Dec;6(6):814-31.
17. Hernandez-Giron C, Smith JS, Lorincz A, Lazcano E, Hernandez-Avila M, Salmeron J. High-risk human papillomavirus detection and related risk factors among pregnant and nonpregnant women in Mexico. Sex Transm Dis. 2005 Oct;32(10):613-8.
18. Papanicolaou GN, Traut HF. The diagnostic value of vaginal smears in carcinoma of the uterus. 1941. Arch Pathol Lab Med. 1997 Mar;121(3): 211-24.
19. Anderson GH, Boyes DA, Benedet JL, Le Riche JC, Matisic JP, Suen KC, et al. Organisation and results of the cervical cytology screening programme in British Columbia, 1955-85. Br Med J (Clin Res Ed). 1988 Apr 2;296(6627):975-8.
20. Morimura Y, Fujimori K, Soeda S, Hashimoto T, Takano Y, Yamada H, et al. Cervical cytology during pregnancy--comparison with non-pregnant women and management of pregnant women with abnormal cytology. Fukushima J Med Sci. 2002 Jun;48(1):27-37.
21. Lurain JR, Gallup DG. Management of abnormal Papanicolaou smears in pregnancy. Obstet Gynecol. 1979 Apr;53(4):484-8.
22. Benedet JL, Selke PA, Nickerson KG. Colposcopic evaluation of abnormal Papanicolaou smears in pregnancy. Am J Obstet Gynecol. 1987 Oct; 157(4 Pt 1):932-7.
23. LaPolla JP, O'Neill C, Wetrich D. Colposcopic management of abnormal cervical cytology in pregnancy. J Reprod Med. 1988 Mar;33(3): 301-6.
24. Baldauf JJ, Dreyfus M, Ritter J, Philippe E. Colposcopy and directed biopsy reliability during pregnancy: a cohort study. Eur J Obstet Gynecol Reprod Biol. 1995 Sep;62(1):31-6.
25. Siddiq TS, Twigg JP, Hammond RH. Assessing the accuracy of colposcopy at predicting the outcome of abnormal cytology in pregnancy. Eur J Obstet Gynecol Reprod Biol. 2006 Jan 1;124(1):93-7.
26. Ostergard DR, Nieberg RK. Evaluation of abnormal cervical cytology during pregnancy with colposcopy. Am J Obstet Gynecol. 1979 Aug 1;134(7):756-8.
27. Jain AG, Higgins RV, Boyle MJ. Management of low-grade squamous intraepithelial lesions during pregnancy. Am J Obstet Gynecol. 1997 Aug;177(2):298-302.
28. Serati M, Uccella S, Laterza RM, Salvatore S, Beretta P, Riva C, et al. Natural history of cervical intraepithelial neoplasia during pregnancy. Acta Obstet Gynecol Scand. 2008;87(12):1296-300.
29. Hannigan EV. Cervical cancer in pregnancy. Clin Obstet Gynecol. 1990 Dec;33(4):837-45.
30. Averette HE, Nasser N, Yankow SL, Little WA. Cervical conization in pregnancy. Analysis of 180 operations. Am J Obstet Gynecol. 1970 Feb 15;106(4):543-9.
31. Daskal JL, Pitkin RM. Cone biopsy of the cervix during pregnancy. Obstet Gynecol. 1968 Jul;32(1):1-5.
32. Hannigan EV, Whitehouse HH, 3rd, Atkinson WD, Becker SN. Cone biopsy during pregnancy. Obstet Gynecol. 1982 Oct;60(4):450-5.
33. Robova H, Rob L, Pluta M, Kacirek J, Halaska M, Jr., Strnad P, et al. Squamous intraepithelial lesion-microinvasive carcinoma of the cervix during pregnancy. Eur J Gynaecol Oncol. 2005;26(6):611-4.
34. Lee RB, Neglia W, Park RC. Cervical carcinoma in pregnancy. Obstet Gynecol. 1981 Nov;58(5):584-9.
35. Van Calsteren K, Vergote I, Amant F. Cervical neoplasia during pregnancy: diagnosis, management and prognosis. Best Pract Res Clin Obstet Gynaecol. 2005 Aug;19(4):611-30.
36. Zemlickis D, Lishner M, Degendorfer P, Panzarella T, Sutcliffe SB, Koren G. Maternal and fetal outcome after invasive cervical cancer in pregnancy. J Clin Oncol. 1991 Nov;9(11):1956-61.
37. Hacker NF, Berek JS, Lagasse LD, Charles EH, Savage EW, Moore JG. Carcinoma of the cervix associated with pregnancy. Obstet Gynecol. 1982 Jun;59(6):735-46.
38. Greer BE, Easterling TR, McLennan DA, Benedetti TJ, Cain JM, Figge DC, et al. Fetal and maternal considerations in the management of stage I-B cervical cancer during pregnancy. Gynecol Oncol. 1989 Jul;34(1): 61-5.
39. Hopkins MP, Morley GW. The prognosis and management of cervical cancer associated with pregnancy. Obstet Gynecol. 1992 Jul;80(1):9-13.
40. Monk BJ, Montz FJ. Invasive cervical cancer complicating intrauterine pregnancy: treatment with radical hysterectomy. Obstet Gynecol. 1992 Aug;80(2):199-203.
41. Baltzer J, Regenbrecht ME, Kopcke W, Zander J. Carcinoma of the cervix and pregnancy. Int J Gynaecol Obstet. 1990 Apr;31(4):317-23.
42. van der Vange N, Weverling GJ, Ketting BW, Ankum WM, Samlal R, Lammes FB. The prognosis of cervical cancer associated with pregnancy: a matched cohort study. Obstet Gynecol. 1995 Jun;85(6):1022-6.
43. Shivvers SA, Miller DS. Preinvasive and invasive breast and cervical cancer prior to or during pregnancy. Clin Perinatol. 1997 Jun;24(2): 369-89.
44. Prem KA, Makowski EL, McKelvey JL. Carcinoma of the cervix associated with pregnancy. Am J Obstet Gynecol. 1966 May 1;95(1):99-108.
45. Sorosky JI, Squatrito R, Ndubisi BU, Anderson B, Podczaski ES, Mayr N, et al. Stage I squamous cell cervical carcinoma in pregnancy: planned delay in therapy awaiting fetal maturity. Gynecol Oncol. 1995 Nov; 59(2):207-10.