Pregnancy with Cervical Cancer

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INTRODUCTION
Cervical cancer is one of the most common cancer in women’s reproductive period. The median age of cervical cancer diagnosed in pregnancy ranging from 7.5 to 45.0 cervical cancers per 100,000 pregnancies. The aim of this review was to provide information about the difficulties in diagnosing and managing cervical cancer during pregnancy. A systematic review of the literature was undertaken using the following words: cervical cancer and pregnancy. The result showed that there was a consensus in the literature regarding diagnosis and management of cervical cancer during pregnancy. However, the management of invasive cervical carcinoma during pregnancy depends on the stage of the disease, the gestational age at diagnosis, and the woman’s desire to continue pregnancy. In conclusion, invasive cervical cancer during pregnancy is rare but is a dilemma for patients and their physicians. The management of invasive cervical carcinoma during pregnancy depends on the situation and condition.

MATERIALS AND METHODS
The present review discusses the current guidelines about cervical cancer associated with pregnancy. A systematic review of literature was undertaken by searching the PubMed, Cochrane, Excerpta Medica (Embase), Literatura Latino Americana e do Caribe em Ciências da Saúde (Lilacs), and Scientific Electronic Library Online (SciELO) databases. The search used the following key words: cervical cancer and pregnancy. Articles were selected according to the following criteria: literature reviews, prospective studies, and case reports presenting approaches for diagnosing cervical cancer during pregnancy, particularly using innovative treatments, protocols, and consensuses from institutions specializing in this disease.

DIAGNOSIS
The presenting symptoms of cervical cancer in pregnant women are the same as in non-pregnant women. Vaginal bleeding is the earliest symptom in both groups. However, pregnant women are more likely to experience cramping, lower abdominal pressure, and back pain. These symptoms may be mistaken as signs of normal pregnancy. A Pap smear is a key diagnostic tool for cervical cancer. In pregnant women, a Pap smear is typically performed at the third trimester. If the smear is abnormal, further testing such as colposcopy or biopsy may be necessary.

Pregnancy with Cervical Cancer: A Systematic Review

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Although infrequent, cervical cancer is the most commonly diagnosed malignancy during pregnancy. The overall incidence of cervical cancer in pregnancy ranging from 7.5 to 45.0 cervical cancers per 100,000 pregnancies. The aim of this review was to provide information about the difficulties in diagnosing and managing cervical cancer during pregnancy. A systematic review of the literature was undertaken using the following words: cervical cancer and pregnancy. The result showed that there was a consensus in the literature regarding diagnosis and management of cervical cancer during pregnancy. However, the management of invasive cervical carcinoma during pregnancy depends on the stage of the disease, the gestational age at diagnosis, and the woman’s desire to continue pregnancy. In conclusion, invasive cervical cancer during pregnancy is rare but is a dilemma for patients and their physicians. The management of invasive cervical carcinoma during pregnancy depends on the situation and condition.

ABSTRACT
Meskipun jarang, kanker serviks merupakan kanker yang paling sering didiagnosis selama kehamilan. Secara keseluruhan kejadian kanker serviks pada kehamilan berkisar 7,5-45,0 kasus kanker serviks per 100.000 kehamilan. Tujuan tinjauan pustaka ini adalah untuk memberikan informasi tentang kesulitan mendiaagnosis dan mengelola kanker serviks selama kehamilan. Peninjauan sistematis literatur dilakukan dengan mengguna-
kan kata-kata berikut: kanker leher rahim dan kehamilan. Hasilnya memperlihatkan bahwa sebenarnya ada konsensus dalam literatur mengenai diagnosis dan manajemen kanker serviks selama kehamilan. Namun, untuk pengelolaan karsinoma invasif, manajemen selama kehamilan tergantung pada stadium penyakit, usia kehamilan saat diagnosis, dan keinginan untuk melanjutkan kehamilan. Simpulan, kanker serviks invasif selama kehamilan jarang tetapi merupakan dilema bagi wanita dan dokter. Pengelolaan karsinoma serviks invasif selama kehamilan ter-
gantung pada situasi dan kondisi.

Key words: cervical cancer, pregnancy, invasive carcinoma

ABSTRAK
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INTRODUCTION
Cervical cancer is one of the most common cancer in women’s reproductive period. The median age of cervical cancer diagnosed in pregnancy ranging from 7.5 to 45.0 cervical cancers per 100,000 pregnancies. The aim of this review was to provide information about the difficulties in diagnosing and managing cervical cancer during pregnancy. A systematic review of the literature was undertaken using the following words: cervical cancer and pregnancy. The result showed that there was a consensus in the literature regarding diagnosis and management of cervical cancer during pregnancy. However, the management of invasive cervical carcinoma during pregnancy depends on the stage of the disease, the gestational age at diagnosis, and the woman’s desire to continue pregnancy. In conclusion, invasive cervical cancer during pregnancy is rare but is a dilemma for patients and their physicians. The management of invasive cervical carcinoma during pregnancy depends on the situation and condition.

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Pregnancy. A patient with an abnormal Pap smear, colposcopic findings and if necessary a targeted cervical biopsy. Evaluation by Papanicolaou (Pap) smear (including endocervical sampling) and biopsy. Conization is a summary of information derived mainly from a bimanual palpatory examination and an ultrasound for fetus viability. Taking a cervical smear for the cytological examination, apart from physical examination and radiologic investigations (Table 2). During pregnancy, decisions regarding the use of radiologic investigations must consider the age of fetus and the estimated dose of radiation delivered. In pregnant patient, ultrasound and MRI should be considered as alternatives to CT scans since both are noninvasive and are not associated with ionizing radiation.

The most frequent histological type of cervical cancer in pregnant women, as in non-pregnant women, is squamous cell carcinoma (80%); less frequently is cervical adenocarcinoma (approximately 11%).

**STAGING**

Stage of the disease during pregnancy is defined according to FIGO classification, which is a summary of information derived mainly from physical examination and radiologic investigations (Table 2). During pregnancy, decisions regarding the use of radiologic investigations must consider the age of fetus and the estimated dose of radiation delivered. In pregnant patient, ultrasound and MRI should be considered as alternatives to CT scans since both are noninvasive and are not associated with ionizing radiation.

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**TREATMENT**

The management of invasive cervical carcinoma during pregnancy depends on the stage of the disease, the gestational age at diagnosis, and the woman’s desire to continue pregnancy. Noninvasive Cervical Carcinoma

Studies have shown that treatment/follow-up of noninvasive carcinoma can be safely deferred until postpartum period, provided that careful colposcopic evaluation is performed in addition to cytology.

**Invasive Cervical Carcinoma**

Surgery

For those patients who were present prior to 20 weeks’ gestation, treatment options include immediate surgery with the fetus left in situ or a delay in treatment to allow for fetal viability and definitive surgery postpartum. In general, there are few reports on delaying therapy in pregnancy. Studies to date have not shown adverse maternal outcomes after treatment delays of 5-40 weeks. Cell type, depth of penetration, and tumor size should be considered in the decision to recommend treatment delay in early disease. It has been suggested that delay can be considered in stages IA1, IA2, and IB1. It is recommended to repeat examination every 6-8 weeks (including colposcopy) until surgery. For higher stages i.e. IB2 and IIA, it should be suggested early treatment.

Concerns regarding the safety of surgery for cervical carcinoma in pregnant patients have been raised. Although increased operative time, blood loss and fistulae formation have been reported, recent studies have not demonstrated an increase in blood transfusion requirements or major complications.

The choice of therapeutic modality for pregnant women with cervical cancer should be decided in the same manner as for non-pregnant patients. The treatment is individualized, based on the stage of the disease according to the International Federation of Gynecology (FIGO), the stage of pregnancy, desire to continue the pregnancy and risks of modifying or delaying cancer treatment during the pregnancy. When the pregnancy is terminated, patient can be treated according to the stage of the disease. In case of continuation of the pregnancy, patient is non-invasively staged with MRI without gadolinium contrast or inva-
sively staged with laparoscopic nodal evaluation when indicated.\textsuperscript{17}

When the patient is diagnosed with carcinoma in situ or stage IA1 disease without Lymphovascular Space Involvement (LVSI), no further treatment is indicated after Large Loop Excision of the Transfer Zone (LLETZ) or conization. For pregnant women with early stage disease (FIGO: IA2, IB1, IIA) diagnosed after 20 weeks of gestation, treatment may be delayed until the fetus has matured. Upon fetal maturation a caesarean section is performed, followed by radical hysterectomy with bilateral pelvic lymphadenectomy and adjuvant radiation treatment when indicated. For patients with cervical cancer stage IB2 after 20 weeks of gestation, it is acceptable to delay treatment for 8 weeks to allow fetal maturation. The treatment options are outlined in Figure 1. In selected patients with stage IA, IB, IIA tumours who have a desire for fertility preservation, radical trachelectomy with lymphadenectomy is an alternative to conventional radical hysterectomy. Antepartum trachelectomy is accompanied by a high rate of fetal loss.\textsuperscript{17,18}

A difficult dilemma arises when fetal immaturity requires prolongation of pregnancy which could negatively affect the mother’s survival. In such cases women should receive a complete evaluation including MRI and (laparoscopic) lymphadenectomy before considering therapy delay. For pregnant women with stage IB1IA and IB–IVA during gestational weeks 1–20, the standard treatment for cervical cancer is radical hysterectomy and chemoradiation respectively with pregnancy termination or spontaneous abortion. Neoadjuvant cisplatin-based chemotherapy in selected cases beyond the first trimester after careful counselling might be an option to allow for fetal maturation. Cisplatin crosses the placenta but more than 10 cases of fetal exposure to the drug without untoward effects have been published.\textsuperscript{17}

**Radiation Therapy**

External beam radiation followed by intracavitary radiation is recommended for early stage invasive carcinoma in pregnant patient as an alternative to surgery. When being administered in first trimester, spontaneous abortion usually occurs at a cumulative dose of 30 – 50 Gy. Treatment in second trimester results in abortion at a higher cumulative dose and less reliable. As with surgery, planned therapy delays (3 – 17 weeks) to await fetal maturity and delivery prior to treatment have not been shown to adversely affect maternal outcome.\textsuperscript{19,20}

**FIGO Stages >IIB**

In the higher stage categories, radiation is optional and consists of external beam irradiation combined with intracavitary brachytherapy as indicated by tumor extent. Recent evidence suggests that cisplatinum-based combined chemo/radiotherapy improves survival for patients with FIGO stages IB2 to IVA.\textsuperscript{14} Experience of this treatment in pregnant patients is generally lacking. The timing of treatment may be affected by gestational age. For a viable fetus, delivery by cesarean section followed by radiation is recommended. For a nonviable fetus, treatment with the fetus in situ is administered. For first trimester pregnancies these reliably results in abortion. In second trimester, it has been recommended that teletherapy followed by hysterotomy be performed as part of the therapy to avoid delivery of a viable but badly damaged neonate. Others have suggested that routine pretherapy uterine evacuation or hysterotomy not be performed due to complications and treatment delays associated with these procedures.\textsuperscript{7,10,16}
Early studies have suggested increased morbidity with radiation treatment in pregnant patients compared to the nonpregnant population. However, with the use of modern techniques and the avoidance of routine pretreatment uterine evacuation, it appears that the complication rates between the two populations are similar. Treatment for cervical cancer that has spread to distant organs is palliative. Various chemotherapeutic agents have been used with varying success. These include cisplatinum, ifosfamide, paclitaxel and irinotecan.15,16

Chemotherapy
Cancer chemotherapeutic drugs are very potent teratogens. Currently, there is very little information on cancer chemotherapy effect on the fetus. The risk of malformations when chemotherapy is administered in the first trimester has been estimated to be around 10% for single agent chemotherapy and 25% for combination chemotherapy. It is generally suggested that chemotherapy be avoided during first trimester, when cells are actively dividing.21-23 The use of chemotherapy during the second and third trimesters increases the risk of low birth weight and intrauterine growth restriction.2 A platinum-based regimen is the most active and is associated with only a slightly increased risk of congenital abnormalities.14 In most of available reports, toxicity to mother is not specified. Dilutional and iron-deficiency anemia during pregnancy combined with chemotherapy-induced cytopenia increases the risk of anemia. Epoietin alfa does not cross the placenta and is safe in pregnant patients with anemia.13 When chemotherapy is administered during pregnancy, delivery timing should take into account the expected bone marrow depression and potential problems such as bleeding or infections. Self-limiting fetal haematopoetic depression has been described and the neonate should be monitored for this complications.24,25

CONCLUSION
Cervical cancer in pregnancy is curable if diagnosed and treated on time i.e. in its early stages. The treatment depends not only on the stage of the disease, but also on the gestational age at diagnosis i.e. on the ability of the fetus to survive outside the uterus at that moment. The patient’s wish to carry pregnancy to term can also significantly postpone the treatment and consequently affect its outcome and result.

REFERENCES