Carcinoma Cervix in Pregnancy-A Challenge for All

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Abstract

Of all the rights of women, to become a mother is greatest. Nature has endowed every woman with the power of procreation. But how, at times, she has to suffer series of obstacles to achieve this goal, challenging her own life. Carcinoma Cervix is the most challenging cancer during pregnancy as the pregnant uterus itself is affected. It’s a challenge for all the mother, the family and the treating physician. Every year, 500000 new cases of invasive ca cervix are diagnosed. Of all cancers that affect women in India, cervical cancer is the second most common.

Disease Burden in Pregnancy

In developed countries, the incidence and mortality have declined over past decades due to increased availability of cancer screening program [1,2]. But, it is still high among developing nations and remains a major cause of cancer death among women of low socioeconomic countries. This strongly links the incidence with the economic development. Incidence rates vary from 0.1 to 12/10,000 pregnancy for carcinoma cervix and 1.30 to 2.7/1000 pregnancies for Cervical Intraepithelial Neoplasia [3]. Ca cervix is not uncommon to be diagnosed these days, during pregnancy [4]. The frequency of cervical cancer during pregnancy is increasing and will continue to increase as long as women will delay child bearing.

Diagnostic Dilemmas

Carcinoma cervix is one cancer in gynaecology that has been diagnosed clinically for ages. Cancer screening programmes are trying to implement this clinical approach from grass root level. Symptoms of carcinoma cervix in pregnancy are no different from non pregnant state. A high index of suspicion is required to diagnose carcinoma cervix in pregnancy. But the diagnosis is still delayed as many of the symptoms of ca cervix mimic normal pregnancy symptoms like some of the symptoms, i.e., bleeding per vaginum can be misdiagnosed as antepartum haemorrhage. Most common presenting complaint is vaginal bleeding followed by vaginal discharge. With advanced disease, symptoms like pelvic/flank pain, sciatica type leg pain may be present. Thus, any patient presenting with these symptoms should be completely evaluated and not neglected.

With the incorporation of cervical cytology in routine prenatal screening tests, many cases are diagnosed at an early stage. Pap smear being the most cost effective method [5]. Evaluating pap smears is more difficult in pregnancy as compared to colposcopic examination. All women with cytologic abnormality should undergo colposcopic examination. Colposcopically directed biopsy is both safe and efficacious, however, ECC is avoided during pregnancy. The FIGO staging system is used for the diagnosis and evaluation of Carcinoma Cervix in pregnancy. Complications due to biopsy in pregnancy like bleeding per vaginum and initiation of preterm labour can occur, but are rare.

Staging the Disease in Pregnancy

Pregnancy not only complicates the treatment plan but also the staging. Staging of Carcinoma Cervix is done according to FIGO staging system and is clinically staged. Clinical staging is difficult during pregnancy due to soft tissue, collagen tissue edema, as well as limitation of X-Ray. To the rescue, MRI is now widely accepted for evaluation of important prognostic factors like lymph node status, tumour volume, and extent of spread that further decides treatment. Some studies have shown comparable result of USG as an alternative of MRI during pregnancy [6]. The general dictum of any radiologic examination during pregnancy is to keep the radiation dose as low as reasonably achievable and best avoided when possible. According to American college of radiology, studies haven’t discovered any deleterious effect of MRI on fetus in any trimester. Gadolinium contrast (Category C) should only be used if absolutely necessary. Cystoscopy and sigmoidoscopy are also safe in pregnancy.

Management Issues

Management of Carcinoma Cervix in pregnancy is still controversial. A malignancy discovered in pregnancy is very difficult to manage as any maternal intervention has to be balanced with fetal well-being. A multidisciplinary approach is required. Important factors to be taken into consideration are stage of cancer, lymph node status, histological type, gestational age, past medical history, past obstetric history, associated obstetrical complication. Most important of all is the wish of patient regarding continuation or termination of pregnancy. Treatment plan has to be individualized according to risk-benefit ratio. Aggressive treatment cannot be implemented as we are dealing with two lives at the same time. Counselling plays a very important role in this scenario. Due to the sensitivity of the issue, all options are to be discussed. Time and tested that pregnancy does not accelerate the natural history of cervical cancer. Treatment is more dependent on the time of diagnosis of disease.

A biopsy confirmed LSIL is to be followed safely throughout pregnancy by cytologic examination in each trimester and revaluated 8-12 weeks postpartum. For HSIL lesions, both cytologic and colposcopic surveillance is required, every 8-12 weeks. Rate of spontaneous regression of lesion is higher after vaginal delivery as compared to caesarean section [7,8]. Regression rate in postpartum period is very high; hence, surveillance is an important tool. If diagnosed in third trimester, fetal maturity is awaited followed by delivery and appropriate treatment.
For stage 1A1, conization is effective treatment. Or pregnancy can be continued till term followed by vaginal delivery and definitive treatment after the delivery. For stage 1A2 or with lymphatic invasion treatment includes hysterectomy, lymphadenectomy and pelvic irradiation. Delivery should be vaginal unless there is obstetric indication for caesarean section. Definitive treatment is delayed until 4-6 weeks after delivery [9].

Stage 1B to higher stages: both radical surgery and radiation therapy offers similar cure rate. If lymph node negative stage 1B<2 cm simple trachelectomy or conization can be done [10]. For lymph node positive and higher stages radical surgery with lymphadenectomy is the best option [11]. When conservative surgical treatment during pregnancy is not possible NACT (neoadjuvant chemotherapy) is an option to achieve disease control until fetal maturation followed by radical hysterectomy postpartum [12]. Cisplatin 50-100 mg/m² is proposed as standard treatment during pregnancy. Chemotherapy should be avoided in pregnancy in first trimester [13]. Before viability external beam teletherapy can be given. For advanced stages like Stage IVA primary pelvic exenteration may be considered for disease not extending to the pelvic side wall, especially if a vesico-vaginal or recto-vaginal fistula is present.

The disadvantage of primary surgical management in Stage IB2 an IIA is the potential need for postoperative therapy to reduce the risk of local recurrence, such as with positive margins or involvement of parametria or nodes. Risk factors associated with local recurrence include lympho-vascular space invasion, and deep cervical stromal invasion. After primary surgical management, 50%-85% of patients with Stages IB2–IIA have indications for adjuvant radiation or chemoradiation. Morbidity is higher when surgery and radiation are combined. The risk of pelvic node involvement increases with tumor size. Primary surgical management is often not recommended for tumors measuring more than 3 cm, to minimize the likelihood of postoperative chemo-radiotherapy and its associated toxicity.

A 31 year study conducted in Philippines concluded that survival rate for Carcinoma cervix was not different from non-pregnant state. Study concluded that survival rate was not affected by pregnancy, mode of delivery [14], mode of treatment and the timing of treatment. But, was majorly determined by the stage of the disease and the nodal metastasis. MRI is most commonly used for evaluating the lymph node status [15]. Sentinel lymph node biopsy is not considered very reliable in advanced stages as compared to early stage cervical cancer. A multicentric phase 2 trial of sentinel lymph node biopsy was conducted in patients of all stages of cervical cancer and sensitivity was found to be very low.

The risk of recurrence after radical surgery is increased in the presence of positive nodes, positive parametria, or positive surgical margins. Adjuvant concurrent chemo radiation (cisplatin with or without 5-fluorouracil) improves overall survival, progression-free survival, and both local and distant recurrences compared with pelvic irradiation alone in such patients [16].

Neonatal Outcome

Most of the studies revealed reassuring long term follow up. Neonatal outcome depends upon the type of treatment and most importantly the time when the treatment is given. It comprises of low birth weight, stillbirths, admission to neonatal intensive care unit, low Apgar score and perinatal mortality [17]. Women with CIN and Carcinoma cervix have a higher baseline risk of prematurity. And the prematurity decides the fetal morbidity and mortality. Prematurity can be prevented by postponing treatment. Deliberate delay of treatment is an option for early stage disease to attain fetal maturity. But not an option for advanced cancers. Patients, receiving chemotherapy, also have an increased risk of prematurity, as well as fetal toxicity. Thus, the best approach is to have an interdisciplinary decision regarding the timing of delivery by obstetrician and neonatologist.

References