# Maternal and Fetal Outcomes in Pregnancies affected by Bone and Soft Tissue Tumors

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## Abstract

**Objective**  This study was aimed to describe perinatal outcome of a cohort of pregnant patients with bone and soft tissue tumors and to compare the current series with our group's previously reported experience.

**Methods**  Pregnant women diagnosed before and during pregnancy were identified, retrospectively, for the years 2004 to 2014. Relevant maternal and neonatal data were collected.

**Results**  Forty-eight patients were identified. Ten cases were diagnosed during pregnancy. Pelvis, abdomen, and extremities were the most common tumor locations. Osteosarcoma, liposarcoma, and Ewing's sarcoma were the most common histological types and comprise more than 50% of the cases. Metastases occurred in nine cases. Most of the cases (60%) were treated surgically during pregnancy and delivery occurred at term. Chemotherapy was delayed until after delivery. There were no perinatal or infant deaths. Patients presented with advanced maternal disease in 18% in previous report (1983–2003) versus 40% in present report (2004–2014). Metastases were present in 40% and maternal death rate was approximately 20% in both cohorts.

**Conclusion**  Pregnant women with bone and soft tissue tumors are candidates for standard surgical management during pregnancy. Other treatments, such as chemotherapy and radiotherapy must be evaluated for each woman on a case-by-case basis. Iatrogenic prematurity was common in our findings.

**Keywords**
► sarcomas
► cancer
► pregnancy
► outcomes
► perinatal

Cancer during pregnancy is rare, affecting a small percentage of women overall (1:1000 pregnancies), with a reported incidence of 0.07 to 0.1% of malignancies.[1–3] Cancer has major implications for the pregnant woman, her offspring, family, and healthcare providers.[3,4] Treatments such as surgery, chemotherapy, and radiation therapy for maternal care have to be weighed against the potential risk to the fetus.[3,4] The optimal management of primary malignant bone and soft tissue tumors (sarcomas) continues to be a source of debate.[3,4] As the presentation of these tumors are rare in pregnancy and involve many aspects of obstetric, oncological, and neonatal care, healthcare providers from many disciplines must participate in the care planning.[4] Experience of the care team, as well as published series of similar cases, can be important elements in providing information to patients, their families and healthcare providers.

The different subtypes of bone and soft tissue tumors that have been reported in association with pregnancy include: osteosarcoma,[4–8] chondrosarcoma,[4,6,9] liposarcoma,[10–12] rhabdomyosarcoma,[13–15] malignant fibrous histiocytoma,[16–18] fibrosarcoma,[19,20] Ewing's sarcoma,[21,22] giant cell tumors,[6,23] and synovial sarcoma.[24–27]

The objective of this study was to examine the maternal and neonatal outcomes of pregnancies in women diagnosed with primary bone and soft tissue tumors treated over a 10-year period at a tertiary referral center for high risk pregnancies and surgical oncology. Another aim was to compare the presented findings (Series 2) with our group's previously reported experience (Series 1)[4] with these tumors during pregnancy, where we identified 17 cases diagnosed during pregnancy over a 20-year period.[4]

## Materials and Methods

Pregnant women diagnosed with primary bone or soft tissue tumors were identified retrospectively for the years 2004 to 2014 at the Centre for Excellence in Women and Infants Health–University of Toronto and its affiliated hospitals Mount Sinai Hospital and University Health Network which are major referral institutions for maternal fetal medicine, orthopedic oncology, and neonatology in South Western Ontario, Canada. Research Ethics Board approval was obtained. We collected relevant maternal and fetal data for all study subjects, including maternal date of birth, age at diagnosis, gravidity, parity, presenting symptoms, morbidity, and mortality. Tumor characteristics such as anatomical location, type, grade, the presence or absence of metastases at diagnosis, treatment modality (surgery, chemotherapy, radiation), and timing of therapy relative to pregnancy were collected. Other pregnancy-related data including gestational age at diagnosis and birth, mode of delivery, and peripartum complications were recorded. Neonatal data included birth weight, Apgar's scores at 1 and 5 minutes, neonatal complications, admission to neonatal intensive care unit (NICU), and placental pathology with attention to the presence of possible placental metastasis, were collected and analyzed.

## Results

We identified 48 pregnant women with a current or prior history of soft tissue and bone tumors during the 10-year study period (2004–2014). The results are summarized in ►Tables 1 and 2. In the present series, 10 patients were diagnosed during pregnancy while the remaining 38 received their diagnosis prior to pregnancy.

For those diagnosed during pregnancy ($n = 10$), the mean maternal age at diagnosis was 32 years (range: 24–39 years). The mean gestational age at diagnosis was 19 weeks (range: 4–32 weeks). The most common presenting symptoms were pain (60%), detection of a mass or swelling (40%), and bleeding (10%). The abdomen and pelvis were the most common anatomical tumor locations (60%). The rate of cesarean birth was 50% among the patients diagnosed during pregnancy and one patient delivered in the community with

loss to follow-up. Seven patients (70%) were delivered before 37 weeks of gestation, mainly to facilitate maternal sarcoma treatment. Five infants (50%) were subsequently admitted to the NICU after birth as a result of iatrogenic prematurity. None of the infants or their placentas had evidence of metastatic disease on postnatal examination.

For those patients diagnosed before pregnancy ($n = 38$), the mean age of the mothers at the time of diagnosis was 24 years, ranging from childhood up to the age of 40 years. The most common presenting symptom was pain (47%). The pelvis and abdomen were the most common anatomical tumor location (57%), followed by the lower (18%) and upper extremities (18%). With regard to perinatal outcomes (►Table 1), 13 patients had caesarean birth (34%). Indications for caesarean birth included failure to progress, fetal malpresentation, abnormal fetal status (nonreassuring fetal status), joint and physical limitations, and maternal request. Four patients (11%) were delivered before 37 weeks of gestation, three had spontaneous preterm labor, and one experienced an unexplained intrauterine fetal demise. There was one case of late-onset intrauterine growth restriction secondary to placental insufficiency later shown on placental pathology. In addition there was one case of a small for gestational age (SGA) infant (9th percentile) delivered at term. Four infants (8%) were admitted to the NICU after delivery, mainly for prematurity. One infant diagnosed with small for gestational age, talipes, unilateral multicystic dysplastic kidney stayed in the NICU for 18 days. Two neonates delivered at 37 weeks gestation (a set of twins in a patient with osteosarcoma) were treated for transient tachypnea of the newborn. Most of infants were delivered after 37 weeks of gestation (55%). None of the infants or their placentas showed evidence of metastatic disease on postnatal examination.

►Table 2 shows the tumor types identified in this series. Osteosarcoma was the most common type of tumor either diagnosed before ($n = 10$, 26%,) or during pregnancy ($n = 2$, 20%). Four osteosarcoma cases had locally advanced disease involving the pelvis or metastases, most commonly affecting the lungs and mediastinum. In two cases of aggressive metastatic angiosarcoma, there was a maternal death occurred at 23 weeks and another in the postpartum period. The majority of patients diagnosed during (60%) or before pregnancy (82%) had surgical intervention; in one case diagnosed during pregnancy, intervention occurred at the time of caesarean delivery. No patients received chemotherapy or radiation while pregnant in this series.

## Discussion

In this series of 48 patients with bone or soft tissue tumors before or during pregnancy, the most common diagnosis was osteosarcoma. Unlike previous studies which show the most common locations to be lower/upper extremities,[4,7,28] the most common tumor location in this study was the pelvis. Other findings include a high cesarean birth rate as well as that of iatrogenic preterm birth.

Counseling pregnant women with concurrent tumor is challenging as each histologic subtype is unique in terms of prognosis and survival depends on the tumor type, stage,

**Table 1** Sarcomas and pregnancy–maternal and perinatal outcomes

| Maternal/perinatal outcomes | 2004–2014(10 y) Total = 48 cases | | | |
| --- | --- | --- | --- | --- |
| | Diagnosed before pregnancy (n = 38) | | Diagnosed during pregnancy (n = 10) | |
| | *n* | % | *n* | % |
| **Presenting symptoms** | | | | |
| Pain | 18 | 47 | 6 | 60 |
| Swelling or mass | 7 | 18 | 4 | 40 |
| Limitation of movements | 5 | 13 | 0 | – |
| Bleeding | 1 | 3 | 1 | 10 |
| Pathologic fracture | 0 | – | 0 | – |
| **Tumor location** | | | | |
| Head and neck | 1 | 3 | 2 | 20 |
| Thorax/chest | 1 | 3 | 0 | – |
| Mediastinum | 0 | – | 1 | 10 |
| Pelvis/abdomen | 20 | 53 | 6 | 60 |
| Upper extremities | 7 | 18 | 0 | – |
| Lower extremities | 7 | 18 | 0 | – |
| Spine | 2 | 5 | 1 | 10 |
| **Diagnosis/prognosis/treatment** | | | | |
| Surgery | 31 | 82 | 6 | 60 |
| Chemotherapy | 18 | 47 | 0 | – |
| Radiotherapy | 10 | 26 | 0 | – |
| Presentation with metastases | 2 | 5 | 4 | 40 |
| Presentation with advanced disease | 0 | – | 4 | 40 |
| Maternal death | 0 | – | 2 | 20 |
| **Perinatal outcome** | | | | |
| Cesarean birth | 13 | 34 | 5 | 50 |
| Vaginal birth | 12 | 32 | 5 | 50 |
| Prematurity < 37 wk | 4 | 11 | 7 | 70 |
| Infants admitted to NICU | 3 | 8 | 5 | 50 |
| Stillbirth | 1 | 3 | 0 | – |

Abbreviations: NICU, neonatal intensive care unit; wk, week; y, year.

grade, location, and operability.[29] Some tumor types are more aggressive, difficult to manage, and have a high risk to metastasize, such as osteosarcoma,[5,8,30] angiosarcoma,[31] and chondrosarcoma,[9,32] whereas benign but locally aggressive tumors, such as giant cell tumor of the bone[4,23,33] are associated with a better prognosis and survival rate.[33]

While we did not identify placental involvement in our cases diagnosed during pregnancy, there are reports in older literature describing placental metastasis and possibly related fetal growth restriction.[13,21,34]

Preterm birth was a common feature in our series. In one case, preterm birth occurred in association with fetal growth restriction and multiple congenital anomalies. However, iatrogenic preterm birth is the major cause of prematurity in cases where the mother required urgent initiation of chemotherapy or radiotherapy.[26,35–37] These findings were in keeping with our previous study.[4] We found that the caesarean birth rate was higher compared with other series.[10,38,39] Among women seeking elective cesarean birth, reasons included perceived physical joint limitations in hips, pelvis, and abdomen.[4]

Pregnant women may safely undergo general anesthesia and surgical interventions for nonobstetric indications as has been reported by others.[40] In our series, antenatal surgical oncology interventions were performed for five patients and another case occurred at the time of cesarean birth. While none of our patients were treated with chemotherapy during pregnancy, with careful assessment and planning such treatment may be possible during gestation in selected women.[36]

Fetal loss was rare, as we identified a single case of sudden unexplained intrauterine fetal demise at 28 weeks, with a

**Table 2** Sarcomas and pregnancy–tumor types

| Tumor Types | 2004–2014 (10 y) Total = 48 cases | | | |
| | Diagnosed before pregnancy (n = 38) | | Diagnosed during pregnancy (n = 10) | |
| | *n* | % | *n* | % |
|---|---|---|---|---|
| Osteosarcoma | 10 | 26 | 2 | 20 |
| Liposarcoma | 7 | 18 | 0 | – |
| Ewing's Sarcoma | 6 | 16 | 0 | – |
| Rhabdomyosarcoma | 3 | 8 | 0 | – |
| Chondrosarcoma | 2 | 5 | 0 | – |
| Gastrointestinal stromal tumor | 1 | 3 | 1 | 10 |
| Fibromyxoid sarcoma | 1 | 3 | 0 | – |
| Angiomyxoma | 1 | 3 | 0 | – |
| Synovial sarcoma | 0 | – | 1 | 10 |
| Fibrosarcoma | 3 | 8 | 2 | 20 |
| Leiomyosarcoma | 1 | 3 | 1 | 10 |
| Endometrial stromal sarcoma | 1 | 3 | 0 | – |
| Giant cell tumor of bone | 2 | 5 | 0 | – |
| Malignant fibrous histiocytoma | 0 | – | 0 | – |
| Angiosarcoma | 0 | – | 2 | 20 |
| Mesothelioma | 0 | – | 1 | 10 |

childhood history of treated rhabdomyosarcoma, but with an otherwise uncomplicated pregnancy course and fetal growth. With regard to maternal death, as *n* other studies, these occurred in relation to advanced tumor metastases.[4] The two patients that presented maternal death in our series occurred in advanced angiosarcoma, diagnosed during pregnancy as mentioned previously. The patient who demised at 23 weeks became inadvertently pregnant when receiving palliative radiotherapy for breast cancer that had metastasized to lungs, mediastinum, liver and pelvis. The patient opted to continue the pregnancy in the hope of reaching viability for her fetus which demonstrated normal growth and anatomy. Unfortunately, the patient succumbed to advanced metastatic disease at 23 weeks of gestation.

Merimsky and Le Cesne[41] reported on the outcomes of 7 pregnant patients. In five of the cases, the diagnosis and treatment of malignancy likely were delayed due to pregnancy. There was one case of prematurity and one small for gestational age infant but otherwise no neonatal complications. The same author describes the outcomes of 13 patients in a more recent article.[42] Most of their patients did not receive surgery until after birth, and none received chemotherapy or radiation during gestation. All patients reported disease progression during pregnancy. The 1-year survival rate was 78%, and the 5-year survival rate was 37.5%, comparable with nonpregnant controls as reported by Huvos et al.[5] One mother in this cohort died from metastatic Ewing's sarcoma.[43]

Molho et al[28] describe women diagnosed with musculoskeletal tumors during pregnancy or immediately after delivery during the period between 1996 and 2006. There were 20 patients, 8 with bone sarcomas and 12 with soft tissue sarcomas. Ten percent of patients were treated surgically by wide excision of the tumor antenatally, and for the remaining patients, therapy was delayed until delivery or termination of pregnancy. Vaginal birth was possible in 45% and caesarean birth was performed in 35%. The rate of spontaneous miscarriage was 5%, while pregnancy was terminated in 15%. Prematurity was reported as 10% of cases but with normal fetal growth and development. This study concluded that sarcomas in pregnancy do not appear to have a significant impact on the maternal prognosis.

While numbers of cases of maternal bone and soft tissue tumors are small, there are some trends our group has noticed over our two study periods, Series 1: 1983 to 2003[4] and Series 2: 2004 to 2014 (►**Table 3**). First, the numbers of cases appear to be increasing suggesting a higher rate of referrals to our tertiary center. In Series 1, we reported 17 cases in 20 years as compared with Series 2, where we noted 48 cases in only 10 years. We noted the maternal presentation with advanced disease was 18% in Series 1 as compared with 40% in Series 2. Rates of metastatic disease (41 vs. 40%) and maternal death (18 vs. 20%) were similar (►**Table 3**).

A significant limitation to our study is the small number of reported cases, a common theme for this area of pregnancy and oncology.[44] Such limited data present a challenge for all healthcare providers caring for pregnant women with rare malignancies, since case reports and small series are the main sources of information that are used in counseling and management.

**Table 3** Sarcomas diagnosed during pregnancy–maternal/
perinatal outcomes and tumor types–comparison between
two series

| Maternal/perinatal outcomes | Series 1 1983–2003 (20 y)[4] n = 17 cases | Series 2 2004–2014 (10 y) n = 10 cases |
|---|---|---|
| | *n (%)* | *n (%)* |
| **Presenting symptoms** | | |
| Pain | 10 (59%) | 6 (60%) |
| Swelling or mass | 8 (47%) | 4 (40%) |
| Bleeding | 0 | 1 (10%) |
| Pathologic fracture | 5 (29%) | 0 |
| **Tumor location** | | |
| Head and neck | 0 | 2 (20%) |
| Mediastinum | 0 | 1 (10%) |
| Pelvis/abdomen | 3 (18%) | 6 (60%) |
| Upper extremities | 6 (35%) | 0 |
| Lower extremities | 8 (47%) | 0 |
| Spine | 0 | 1 (10%) |
| **Diagnosis/prognosis/ treatment[a]** | | |
| Surgery | 9 (53%) | 6 (60%) |
| Presentation with metastases | 7 (41%) | 4 (40%) |
| Presentation with advanced disease | 3 (18%) | 4 (40%) |
| Maternal death | 3 (18%) | 2 (20%) |
| **Perinatal outcome[b]** | | |
| Cesarean birth | 3 (18%) | 5 (50%) |
| Vaginal birth | 13 (76%) | 5 (50%) |
| Prematurity < 37 wk | 4 (22%) | 7 (70%) |
| Infants admitted to NICU | 4 (22%) | 5 (50%) |
| **Tumor types** | | |
| Osteosarcoma | 5 (29%) | 2 (20%) |
| Chondrosarcoma | 4 (24%) | 0 |
| Gastrointestinal stromal tumor | 0 | 1 (10%) |
| Angiomyxoma | 2 (12%) | 0 |
| Synovial sarcoma | 0 | 1 (10%) |
| Fibrosarcoma | 0 | 2 (20%) |
| Leiomyosarcoma | 1 (6%) | 1 (10%) |
| Giant cell tumor of bone | 4 (24%) | 0 |
| Malignant fibrous histiocytoma | 1 (6%) | 0 |
| Angiosarcoma | 0 | 2 (20%) |
| Mesothelioma | 0 | 1 (10%) |

Abbreviations: NICU, neonatal intensive care unit; wk, week; y, year.
[a]No patients in either series received chemotherapy or radiotherapy during pregnancy.
[b]There were no stillbirths in either series.

The American College of Obstetrics and Gynecology (ACOG) recommends that a pregnant woman should never be denied indicated surgery, regardless of trimester.[45] While surgical intervention for the mother should not be delayed due to pregnancy or gestation, treatments such as chemotherapy and radiotherapy require specialized consideration and counseling.[36] With regard to delivery, vaginal birth is preferable unless obstetric factors dictate the need for a caesarean delivery. Iatrogenic prematurity appears to be the major fetal risk factor for patients with bone and soft tissue tumors during pregnancy. We suggest a multidisciplinary approach to manage these patients and to provide a thorough counseling from multiple involved teams including maternal-fetal medicine, medical and surgical oncology, obstetric anesthesia, neonatology, mental health, and social services to help and support the patient and her family through the challenges posed by a cancer diagnosis, in the context of pregnancy.

In summary, this study demonstrates the heterogeneity of bone and soft tissue tumor types that can precede or complicate ongoing pregnancies, as well as the complexity of presentation and management of these patients. Coordination of care within the healthcare team will include obstetricians, surgeons, oncologists, and neonatologists among others.

Précis
Pregnant women with sarcoma are candidates for surgical management during pregnancy. Chemotherapy and radiotherapy must be evaluated individually. Iatrogenic prematurity is a prominent risk.

Conflict of Interest
The authors declare no conflict of interest

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