Characteristics of the Offspring of Women with a History of Malignancy, Excluding Congenital Malformations

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Abstract

Objective: To study the characteristics (except congenital malformations) of offspring born to women with a history of malignancy.

Methods: Data were obtained by linkage between four different Swedish national health registers. We compared the offspring born between 1994 and 2011 of women with a history of malignancy with all other infants. Survival of the infants was followed up through 2013. Adjusting for confounders was performed using Mantel-Haenszel methodology. We identified 7315 infants born to women with a history of a malignancy diagnosed at least 1 year before delivery. The total number of deliveries in Sweden in these years was 1 746 870, with 1 780 112 infants being born. We assessed rates of intrauterine death, preterm birth, low birth weight, and the nature of intrauterine growth. We also examined neonatal diagnoses (asphyxia, chronic respiratory condition, intracranial hemorrhage, jaundice, hypoglycemia, CNS symptoms) and infant death.

Results: In women with a history of malignancy, we found no significantly increased risk for stillbirth or infant death. There were elevated rates of preterm birth (OR 1.50, 95% CI 1.37 to 1.64), very preterm birth (OR 1.89, 95% CI 1.54 to 2.32), and low birth weight (OR 1.50, 95% CI 1.34 to 1.68). There was a significantly increased risk of birth asphyxia, jaundice, hypoglycemia, and low Apgar score among infants born to women with a history of malignancy (OR 1.24, 95% CI 1.15 to 1.33), and this risk was maintained after excluding infants born after IVF.

Conclusion: We found an increased risk of preterm birth and low birth weight among infants of women with a history of malignancy, and as a result, found an increased risk of neonatal morbidity. No significant increase in risk of intrauterine or postnatal death was noted.

Key Words: Malignant disease, offspring, stillbirth, preterm, neonatal morbidity

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Résumé

Objectif : Étudier les caractéristiques (sauf les malformations congénitales) des nourrissons dont la mère a des antécédents de pathologie maligne.

Méthodologie : Les données proviennent de la mise en commun de quatre registres nationaux de santé suédois. Nous avons comparé les nourrissons nés entre 1994 et 2011 dont la mère a des antécédents de pathologie maligne et tous les autres nouveau-nés. Nous avons suivi leur survie jusqu'en 2013 et tenu compte des variables parasites à l'aide de la méthode de Mantel-Haenszel. Nous avons recensé 7 315 nourrissons dont la mère a eu un diagnostic de pathologie maligne au moins un an avant l'accouchement. Entre 1994 et 2011, il y a eu 1 746 870 accouchements en Suède, pour un total de 1 780 112 naissances. Nous avons calculé les taux de décès in utero, de prématurité et de faible poids à la naissance, et avons évalué le développement intra-utérin. Nous nous sommes aussi intéressés aux diagnostics néonataux (asphyxie, affection respiratoire chronique, hémorragie intracrânienne, ictère, hypoglycémie, symptômes du système nerveux central) et à la mortalité infantile.

Résultats : Nous n'avons relevé aucune augmentation significative du risque de mortinaissance et de mortalité infantile chez les femmes présentant des antécédents de pathologie maligne. Toutefois, leurs enfants présentaient un taux élevé de prématurité (RC : 1,50; IC à 95 % : 1,37−1,64), de grande prématurité (RC : 1,89; IC à 95 % : 1,54−2,32) et de faible poids à la naissance (RC : 1,50; IC à 95 % : 1,34−1,68). Ils avaient aussi un risque significativement supérieur d'asphyxie des nouveau-nés, d'ictère et d'hypoglycémie ainsi qu'un faible indice d'Apgar (RC : 1,24; IC à 95 % : 1,15−1,33) − même en excluant les nouveau-nés conçus par fécondation in vitro.

Conclusion : Chez les nourrissons dont la mère a des antécédents de pathologie maligne, nous avons relevé un risque accru de prématurité et de faible poids à la naissance, ce qui cause une augmentation du risque de morbidité néonatale. Toutefois, aucune hausse significative du risque de décès in utero ou postnatal n'a été observée.

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INTRODUCTION

Due to improvements in diagnostic methods and treatment of women with malignant diseases during recent decades, survival rates have increased and pregnancies have become more prevalent in this group.[1] Malignancies and their management may affect the outcome of pregnancy and the health of the offspring. Women with a history of malignancy before pregnancy are understandably concerned about the effect of the malignancy and its treatment on any future pregnancy and on the health of any future offspring.[2,3]

There have been several studies of pregnancy outcome and the health of offspring of survivors of various types of malignancy. Mostly these have been limited to the offspring of survivors of childhood cancer.[4–10] The most constant finding has been an increased risk of preterm birth and low birth weight.[11–13] Haggar et al.[11] studied obstetric and perinatal outcomes of first completed pregnancies (n=1894) in female survivors of adolescent and young adult cancer. In a population-based study in Finland, Madanat-Harjuoja et al.[12] examined the outcomes of deliveries in 1309 female cancer survivors (diagnosed at age 0 to 34 years). Clark et al.[13] examined obstetric and neonatal outcomes in 917 Scottish women with a prior episode of cancer.

In general, no increase in the risk of perinatal death has been noted.[11,14] However, one exception was in a study by Signorello et al.,[15] who found an increased risk of stillbirth and neonatal death after uterine and ovarian irradiation at doses greater than 10 Gy.

In a previous study of the same cohort used in the present study, we explored maternal characteristics and maternal complications during pregnancy and delivery.[16] In that study we identified evidence of subfertility and an increased risk of complications of pregnancy and delivery in women with a history of malignancy. These complications may have a negative impact on the offspring. In the present study we investigated the outcomes for the offspring, except for the presence of congenital malformations, which will be reported subsequently.

METHODS

As described in our previous study,[16] we used the following three national registers to identify and characterize women who gave birth after a previous malignancy: the Swedish Medical Birth Register, the Swedish IVF Register, and the Swedish Cancer Register. The survival of infants was followed up using the Swedish Cause of Death Register through 2013.

Table 1. Number of infants whose mothers had a malignancy at least 1 year before delivery, according to type of malignancy

Malignancy group	Number of infants	Observed (expected) number of stillbirths
Respiratory, digestive, urinary tract cancer	865	1 (3.2)
Skin cancer	1588	8 (5.7)
Breast cancer	404	1 (1.7)
Eye and nervous system cancer	1000	7 (3.4)
Bone and soft tissue malignancy	342	1 (1.4)
Hematological malignancy	1280	4 (4.5)
Ovarian cancer	281	0 (1.0)
Cervical cancer	327	2 (1.3)
Thyroid cancer	680	3 (2.6)
Other malignancy	548	4 (2.5)
Total	7315	31

NOTE: The expected number of stillbirths was calculated from all births and adjusted for year of birth, maternal age, parity, smoking, and BMI.

Each of these registers use the unique personal identification number that is assigned to every person living in Sweden. The National Board of Health and Welfare replaced these identification numbers with unique but unidentifiable numbers that were subsequently used for further linkage between the registers.

The distribution of the diagnoses of the malignant diseases (each woman had only one such diagnosis) was given in our previous study.[16] The subgroups are also shown in Table 1.

The Swedish Cancer Registry does not include any treatment data. However, the various diagnostic groups can be expected to have received a certain type of oncological treatment; for example, skin cancers are typically treated with surgery alone, whereas hematological malignancies most likely are treated with chemotherapy.

The following neonatal characteristics or diagnoses were studied:

1. Preterm births (< 37 weeks) and very preterm births (< 32 weeks) in singletons (in most cases, pregnancy duration was based on results of second trimester sonography)